POCKET NOTEBOOK

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POCKET CARDIOLOGY

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Preface

With *Pocket Cardiology,* we now offer those taking care of patients with complex cardiovascular disease a focused and concise reference to aid them in their daily clinical care. *Pocket Cardiology* has been designed to either supplant the Cardiology section in *Pocket Medicine* or serve as a stand-alone handbook. *Pocket Cardiology* provides greatly expanded coverage of the latest treatment options for the major common cardiovascular diseases as well as new sections on advanced heart failure, vascular, and electrophysiology topics.

We have incorporated key references to the most recent high-tier reviews and important studies published right up to the time *Pocket Cardiology* went to press. We welcome any suggestions for further improvement. Although the recommendations herein are as evidence based as possible, sound clinical judgement must be applied to every scenario.

This book would not have been possible without the help of Melinda Cuerda, who shepherded the project from start to finish, with an incredible eye to detail to ensure that each page of this book was the very best it could be.

It is a privilege to take care of patients, especially when working with the house officers, fellows, and attendings at Brigham and Women's Hospital and the Massachusetts General Hospital. The rapid advances in cardiovascular medicine are truly amazing. We hope the information contained within *Pocket Cardiology* proves useful in your quest to deliver the best possible care to your patients.

Marc S. Sabatine, MD, MPH

Coronary Disease

ELECTROCARDIOGRAPHY

Approach *(a systematic approach is vital)*

- **Rate** (? tachy or brady)
- **Rhythm** (? P waves, ? relationship between P and QRS, ? regular)
- **Intervals** (PR, QRS, QT) and **axis** (? LAD or RAD)
- **Chamber abnormality** (? LAA and/or RAA, ? LVH and/or RVH)
- **QRST changes** (? Q waves, poor R-wave progression V_1-V_6, ST ↑/↓ or T-wave Δs)

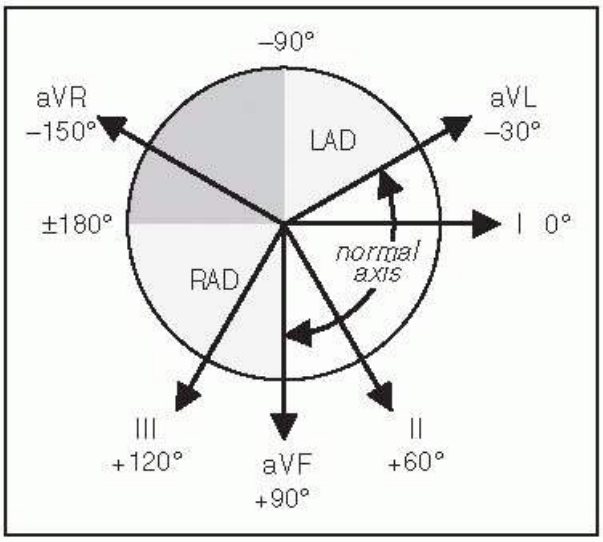


Figure 1-1 QRS axis

Left axis deviation (LAD)

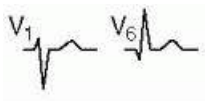
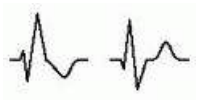
- **Definition:** axis beyond -30° (S > R in lead II)
- **Etiologies:** LVH, LBBB, inferior MI, WPW
- **Left anterior fascicular block (LAFB):** LAD (-45 to -90°) *and* qR in aVL *and* QRS <120 msec *and* no other cause of LAD (eg, IMI)

Right axis deviation (RAD)

- **Definition:** axis beyond +90° (S > R in lead I)
- **Etiologies:** RVH, PE, COPD (usually not > + 110°), septal defects, lateral MI, WPW
- **Left posterior fascicular block (LPFB):** RAD (90-180°) *and* rS in I & aVL *and* qR in III & aVF *and* QRS <120 msec *and* no other cause of RAD

Bundle Branch Blocks (*Circ* 2009;119:e235)

Initial depol. is left-to-right across septum (r in V_1 & q in V_6; nb, absent in

Normal		LBBB) followed by LV & RV free wall, with LV dominating (nb, RV depol. later and visible in RBBB).
RBBB		1. QRS ≥120 msec (110-119 = incomplete) 2. rSR' in R precordial leads (V_1, V_2) 3. Wide S wave in I and V_6 4. ± ST↓ or TWI in R precordial leads
LBBB		1. QRS ≥120 msec (110-119 = incomplete) 2. Broad, slurred, monophasic R in I, aVL, V_5-V_6 (± RS in V_5-V_6 if cardiomegaly) 3. Absence of Q in I, V_5 and V_6 (may have narrow q in aVL) 4. Displacement of ST & Tw opposite major QRS deflection 5. ± PRWP, LAD, Qw's in inferior leads

Bifascicular block: RBBB + LAFB/LPFB. Trifascicular block: bifascicular block + 1° AVB (nb, misnomer as 1° AVB involves AV node but no fascicle per se).

Prolonged QT interval (*NEJM* 2008;358:169; www.torsades.org)

- QT measured from beginning of QRS complex to end of T wave (measure longest QT)
- QT varies w/ HR → corrected w/ Bazett formula: QTc = QT/$\sqrt{RR}$ (RR in sec, can be estimated by 60/HR), overcorrects at high HR and undercorrects at low HR (nl QTc <440 msec ♂ and <460 msec ♀)
- Fridericia's formula preferred at very high or low HR: QTc = QT/ $\sqrt[3]{RR}$
- QT prolongation a/w ↑ risk TdP (espec >500 msec); perform baseline/serial ECGs if using QT prolonging meds, no estab guidelines for stopping Rx if QT prolongs
- Etiologies:

  Antiarrhythmics: class Ia (procainamide, disopyramide), class III (amio, sotalol, dofet)

  Psych drugs: antipsychotics (phenothiazines, haloperidol, atypicals), Li, ? SSRI, TCA

  Antimicrobials: macrolides, quinolones, azoles, pentamidine, atovaquone, atazanavir

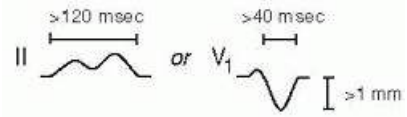
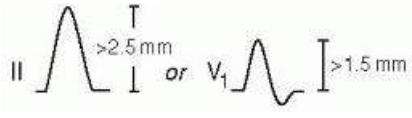
  Other: antiemetics (droperidol, 5-HT3 antagonists), alfuzosin, methadone, ranolazine

  Electrolyte disturbances: hypoCa (nb, hyperCa a/w ↑ QT), ± hypoK, ? hypoMg

  Autonomic dysfxn: ICH (deep TWI), stroke, carotid endarterectomy, neck dissection

  Congenital (long QT syndrome): K, Na, & Ca channelopathies (*Circ* 2013;127:126)

  Misc: CAD, CMP, bradycardia, high-grade AVB, hypothyroidism, hypothermia, BBB

ECG P-wave Criteria	**Left Atrial Abnormality (LAA)** 	**Right Atrial Abnormality (RAA)** 

Left ventricular hypertrophy (LVH) (*Circ* 2009;119:e251)

- Etiologies: HTN, AS/AI, HCMP, coarctation of aorta
- Criteria (all w/ Se <50%, Sp >85%; accuracy affected by age, sex, race, BMI)

  Romhilt-Estes point-score system (4 points = probable; 5 points = diagnostic):

Criteria	Points
Voltage (any of the following): R or S in limb leads ≥20 mm; S in V_1 or V_2 ≥30 mm; R in V_5 or V_6 ≥30 mm	3
ST-T displacement opposite to QRS deflection (either):	
◦ Pt not on digoxin	3
◦ Pt on digoxin	1
Left atrial enlargement	3
Left axis deviation	2
QRS duration ≥90 msec	1
Delayed intrinsicoid deflection (QRS onset to R peak) in V_5 or V_6 >50 msec	1

  Sokolow-Lyon: S in V_1 + R in V_5 or V_6 ≥35 mm or R in aVL ≥11 mm

  Cornell: R in aVL + S in V_3 >28 mm in men or >20 mm in women If LAD/LAFB, S in III + max (R+S) in precordium ≥30 mm

Right ventricular hypertrophy (RVH) (*Circ* 2009;119:e251)

- Etiologies: cor pulmonale, congenital (tetralogy, TGA, PS, ASD, VSD), MS, TR
- Criteria (all tend to be insensitive, but highly specific, except in COPD) R > S in V_1 or R in V_1 ≥7 mm, S in V_5 or V_6 ≥7 mm, drop in R/S ratio across precordium RAD ≥+110° (LVH + RAD *or* prominent S in V_5 or V_6 → *biventricular* hypertrophy)

Ddx of dominant R wave in V_1 or V_2

- Ventricular enlargement: RVH (RAD, RAA, deep S waves in I, V_5, V_6); HCMP
- Myocardial injury: posterior MI (anterior Rw = posterior Qw; often with IMI)
- Abnormal depolarization: RBBB (QRS > 120 msec, rSR'); WPW (↓ PR, δ wave, ↑ QRS)

- Other: dextroversion; Duchenne muscular dystrophy; lead misplacement; nl variant

Poor R wave progression (PRWP) (*Am Heart J* 2004;148:80)

- Definition: loss of anterior forces w/o frank Q waves (V_1-V_3); R wave in V_3 ≤3 mm
- Possible etiologies (nonspecific):

  old anteroseptal MI (usually w/ R wave V_3 ≤1.5 mm, ± persistent ST ↑ or TWI V_2 & V_3) cardiomyopathy

  LVH (delayed RWP with prominent left precordial voltage), RVH, COPD (which may also have RAA, RAD, limb lead QRS amplitude ≤5, $S_I S_{II} S_{III}$ w/ R/S ratio <1 in those leads)

  LBBB; WPW; clockwise rotation of the heart; lead misplacement; PTX

Pathologic Q waves

- Definition: ≥30 msec (≥20 msec V_2-V_3) or >25% height of R wave in that QRS complex
- Small (septal) q waves in I, aVL, V_5 & V_6 are nl, as can be isolated Qw in III, aVR, V_1
- "Pseudoinfarct" pattern may be seen in LBBB, infiltrative dis., HCM, COPD, PTX, WPW
- In WPW, Qw pattern may help localize site of accessory pathway (Bundle of Kent)

ST elevation (STE) (*NEJM* 2003;349:2128; *Circ* 2009;119:e241 & e262)

- **Acute MI** (upward convexity ± TWI) or prior MI with persistent STE
- **Coronary spasm** (Prinzmetal's angina; transient STE in a coronary distribution)
- **Pericarditis** (diffuse, upward concavity STE; a/w PR ↓ ; Tw usually upright)
- **HCM, Takotsubo CMP, ventricular aneurysm,** cardiac contusion
- **Pulmonary embolism** (occ. STE V_1-V_3; classically a/w TWI V_1-V_4, RAD, RBBB, $S_1Q_3T_3$)
- **Repolarization abnormalities**

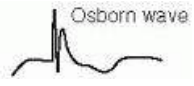
  LBBB (↑ QRS duration, STE discordant from QRS complex) dx *of* MI *in setting of* LBBB*:* Sgarbossa criteria (*NEJM* 1996;334:481) ≥1 mm STE concordant w/ QRS (Se 73%, Sp 92%) STD ≥1 mm V_1-V_3 (Se 25%, Sp 96%) STE ≥5 mm discordant w/ QRS (Se 31%, Sp 92%)

  LVH (↑ QRS amplitude)

  Brugada syndrome (rSR', downsloping STE V1-V2; Na channelopathy a/w SCD)

  Hyperkalemia (see below)

  Hypothermia: Osborn waves

  ⊕ deflection at J point, typically in R-precordial leads 

proportional to degree of hypothermia
- **aVR:** STE > 1 mm a/w ↑ mortality in STEMI; STE aVR > V_1 a/w left main disease
- **Early repolarization:** most often seen in V_2-V_5 in young adults (*JACC* 2015;66:470)

  1-4 mm elev of peak of notch or start of slurred downstroke of R wave (ie, J point); ± up concavity of ST & large Tw (∴ ratio of STE/T wave <25%; may disappear w/ exercise)

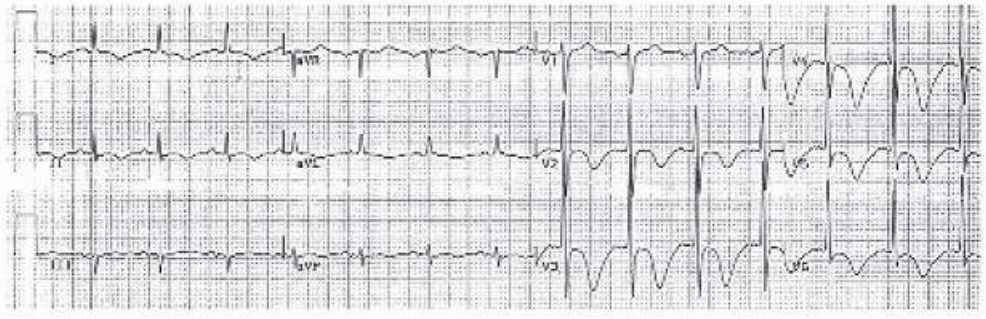
? early repol in inf leads may be a/w ↑ risk of VF (*NEJM* 2009;361:2529; *Circ* 2011;124:2208)

ST depression (STD)

- **Myocardial ischemia** (± Tw abnl) or acute true posterior MI (V_1-V_3)
- Digitalis effect (downsloping ST ± Tw abnl, does *not* correlate w/ dig levels)
- Hypokalemia (± U wave)
- Repolarization abnl in a/w LBBB or LVH (usually in leads V_5, V_6, I, aVL)

T wave inversion (TWI; generally ≥1 mm; deep if ≥5 mm) (*Circ* 2009;119:e241)

- Ischemia or infarct; *Wellens' sign* (deep, symmetric precordial TWI) → proximal LCA lesion

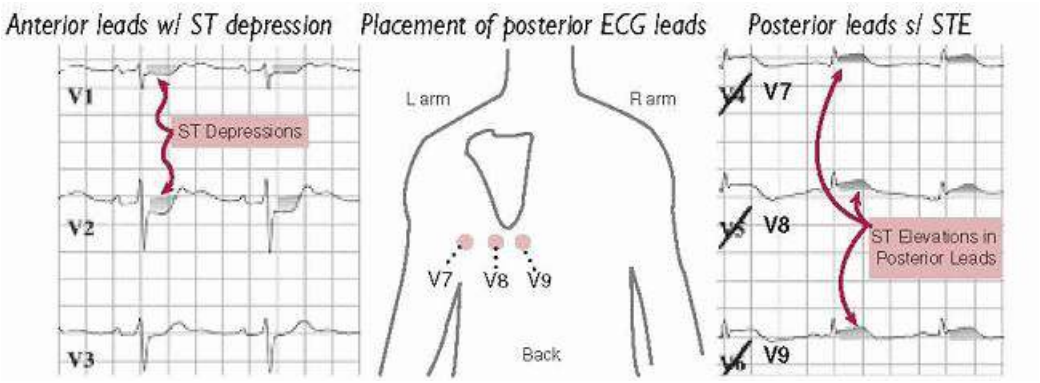


(Wellens' sign, from Cuculich PS and Kates AM. *The Washington Manual Cardiology Subspecialty Consult,* 3rd ed. Philadelphia: Wolters Kluwer Health, 2014:286.)

- Myopericarditis; CMP (Takotsubo, ARVC, apical HCM); MVP; PE (espec if TWI V_1-V_4)
- Repolarization abnl in a/w LVH/RVH ("strain pattern"), BBB
- Posttachycardia or postpacing
- Electrolyte, digoxin, PaO_2, $PaCO_2$, pH or core temperature disturbances
- Intracranial bleed ("cerebral T waves," usually w/ ↑ QT)
- Normal variant in children (V_1-V_4) and leads in which QRS complex predominantly ⊖

True posterior MI (posterior STE appearing as anterior STD)

- STD ± ↑ R wave in leads V1-V4 may correspond to acute posterior "ST-elevation" MI
- ✓ Posterior ECG leads; manage as a STEMI with rapid reperfusion



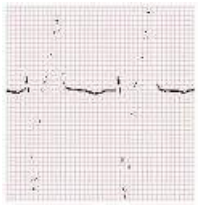
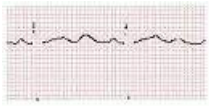
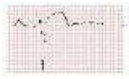
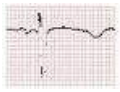
(Modified from Martindale JL, Brown DFM. *Rapid Interpretation of ECGs in Emergency Medicine*. Philadelphia:

Lippincott Williams & Wilkins, 2012:364,376)

Low voltage

- QRS amplitude (R + S) <5 mm in all limb leads & <10 mm in all precordial leads
- Etiologies: COPD (precordial leads only), pericardial effusion, myxedema, obesity, pleural effusion, restrictive or infiltrative CMP, diffuse CAD

Electrolyte Abnormalities

→ **K**	Tented Tw, ↓ QT Small Pw, ↑ PR, AVB Wide QRS → sinusoidal pattern STE (typically V_1-V_2)	
→ **K**	Flattened Tw U waves (⊕ deflection after T) ST depression Ectopy; ↑ QT & TdP	
↑ **Ca**	↓ QT, flattened Tw & Pw J point elevation	
↓ **Ca**	↑ QT; Tw Δs	

(ECGs modified from Wagner GS, Strauss DG. *Marriott's Practical Electrocardiography*, 12th ed. Philadelphia: Lippincott Williams & Wilkins, 2014)

CHEST PAIN

Disorder	Typical Characteristics & Diagnostic Studies
	Cardiac Causes
ACS (15-25% of chest pain in ED)	Substernal pressure radiating to neck, jaw, arm. ± Dyspnea, diaphoresis, N/V; a/w exertion; ↓ w/ NTG or rest; however, not reliable indicator (*Annals EM* 2005;45:581). ± ECG Δs: STE, STD, TWI, Qw. ± ↑ Troponin.
Pericarditis & myo-pericarditis	Sharp pain → trapezius, ↑ w/ respiration, ↓ w/ sitting forward. ± Pericardial friction rub. ECG Δs (diffuse STE & PR ↓, opposite in aVR) ± pericardial effusion. If myocarditis, same as above + ↑ Tn and ± s/s HF and ↓ EF.

Aortic dissection	Abrupt-onset severe tearing, knifelike pain (absence ⊖ LR 0.3), ant or post midscapular. HTN or HoTN. ± Asymmetric (> 20 mmHg) BP or pulse deficit (⊕ LR 5.7), focal neuro deficit (⊕ LR >6), AI, widened mediastinum on CXR (absence ⊖ LR 0.3); false lumen on imaging. (*JAMA* 2002;287:2262)
	Pulmonary Causes
Pneumonia	Pleuritic; dyspnea, fever, cough, sputum. ↑ RR, crackles. CXR infiltrate.
Pleuritis	Sharp, pleuritic pain. ± Pleuritic friction rub.
PTX	Sudden onset, sharp pleuritic pain. Hyperresonance, ↑ BS. PTX on CXR.
PE	Sudden onset pleuritic pain. ↑ RR & HR, ↓ S_aO_2, ECG Δs (sinus tach, RAD, RBBB, $S_IQ_{III}T_{III}$, TWI V_1-V_4, occ STE V_1-V_3). ⊕ CTA or V/Q.
Pulm HTN	Exertional pressure, DOE. ↓ S_aO_2, loud P_2, RV heave, right S_3 and/or S_4.
	GI Causes
Esophageal reflux	Substernal burning, acid taste in mouth, water brash. ↑ by meals, recum-bency; ↑ by antacids. EGD, manometry, pH monitoring.
Esoph spasm	Intense substernal pain. ↑ by swallowing, ↓ by NTG/CCB. Manometry.
Mallory-Weiss	Esophageal tear precipitated by vomiting. EGD.
Boerhaave syndrome	Esoph. rupture typically precipitated by vomiting. Severe pain, ↑ w/ swallowing. Palpable SC emphysema; mediastinal air on chest CT.
PUD	Epigastric pain, relieved by antacids. ± GIB. EGD, ± *H. pylori* test.
Biliary dis.	RUQ pain, N/V. ↑ by fatty foods. RUQ U/S; ↑ LFTs.
Pancreatitis	Epigastric/back discomfort. ↑ amylase & lipase; abd CT.
	Musculoskeletal and Miscellaneous Causes
Costochond	Localized sharp pain. ↑ w/ movement. Reproduced by palpation.
Zoster	Intense unilateral pain. Pain may precede dermatomal rash.
Anxiety	"Tightness," dyspnea, palpitations, other somatic symptoms

(*Braunwald's Heart Disease*, 10th ed, 2014)

Initial approach

- **Focused history:** quality & severity of pain; location & radiation; provoking & palliating factors; intensity at onset; duration, frequency & pattern; setting in which it occurred; associated sx; cardiac hx and risk factors

Pain Feature	Classic for ACS	Atypical for ACS
Quality	Pressure (⊕ LR 1.3), tightness, "Levine" sign (clenched fist over chest), squeezing, fullness, heavy weight, more than prior angina or ≈ prior MI (⊕ LR 1.8)	Sharp (⊕ LR 0.3)
Region/radiation	Substernal, radiating to L or R arm or shoulder (⊕ LR 2.3-4.7), jaw, teeth, neck	Small area, points w/ 1 finger, radiation to back
Provocation	Exertion (⊕ LR 2.4; but may be absent)	Pleuritic, positional or w/ palp (⊕ LR ≤0.3), eating
Associated sx	Diaphoresis (⊕ LR 2.0), N/V (⊕ LR 1.9), dyspnea	

(*JAMA* 2005;294:2623)

- **Targeted exam:** VS (including BP in both arms), cardiac gallops, murmurs or rubs; signs of vascular disease (carotid or femoral bruits, ↓ pulses), signs of heart failure; lung & abdominal exam; chest wall exam for reproducibility of pain
- **12-lead ECG:** obtain w/in 10 min; c/w priors & obtain serial ECGs. In addition, consider:

  posterior leads (V_7-V_9; remove V4-V6 and place in post axillary, mid-clavic & L paraspinal position) useful to ✓ for posterior STEMI if hx c/w ACS but stnd ECG unrevealing, espec if ST ↓ V_1-V_4 (ant ischemia vs post STEMI) or R/S V_1-V_2 > 1

  R-sided leads (place V_3-V_6 in mirror image position on R side of chest) in inferior STEMI to detect RV involvement

- **CXR;** other imaging (echo, PE CTA, etc.) as indicated based on H&P and initial testing
- **Biomarkers** (see below): Tn preferred biomarker, ✓ at baseline & 3-6 h after sx onset

Biomarkers

- **Troponin:** level >99th %ile w/ rise & fall in approp. setting is dx of MI; >95% Se, 90% Sp Detectable 1-6 h after injury, peaks 24 h, may remain elevated for 7-14 d in STEMI Tn may be ↑ in CKD in absence of ACS, ∴ add CK-MB/serial Tn for confirmation *Sensitive* Tn assays: 98% Se, 90% Sp, 75% PPV, 99% NPV w/in 3 h of admit to ED, 82% Se & 95% NPV at time of admission to ED (*JAMA* 2011;306:2684)

  High-sensitivity Tn assays quantify Tn in majority of healthy individ.; prog value in asx general pop., stable CAD & DM (*NEJM* 2009;361:2538 & 2015;373:610; *JAMA* 2010;304:2503)

- **CK-MB:** less Se & Sp than Tn for dx of MI

  Sources include skeletal muscle, tongue, diaphragm, intestine, uterus, prostate

  CK-MB relative index (ratio of CK-MB to CK) >2.5-3 suggests cardiac vs skel. muscle

  CK-MB begins to rise 4-6 h post MI (may take 12 h) and returns to baseline w/in 36-48 h

  May aid in gauging timing of MI (⊕ Tn & ⊖ CK-MB suggests MI several days ago)

  May help dx reinfarction if Tn already elevated; however, Tn should ↑ as well

- Myoglobin & heart-type fatty acid binding protein are smaller molecules that may appear in circulation as early as 30 min after MI, but lack of specificity limits utility

- **D-dimer:** low level useful to r/o PE (qv) and aortic dissection (qv)

- B-type natriuretic peptide (BNP): elevations not specific for ACS but suggest ↑ ventricular wall stress seen not only in decompensated HF, but also ACS & PE

Interpretation of elevated cardiac biomarkers (troponin or CK-MB)

- *Does it reflect true myocardial injury?* Almost always the case for Tn; CK-MB less specific.

- *If myocardial injury, what is the pathobiology?* Ddx includes:

  MI (injury due to ischemia): rise and/or fall in cardiac biomarker (preferably Tn)

  >99th %ile w/ ≥1 of the following:

  1) sx of ischemia

  2) new Qw

  3) new STΔ or LBBB

  4) intracoronary thrombus

  5) imaging evidence of new loss of myocardium or regional wall motion abnl non-ischemic injury (eg, myocarditis/toxic CMP, cardiac contusion) multifactorial (eg, PE, sepsis, severe HF, renal failure, Takotsubo, infiltrative disease)

- *If* MI*, what type?* (*Circ* 2012;126:2020)

Type	Descriptor	Features
1	Spontaneous	Pathologic process in wall of coronary artery (eg, plaque rupture) resulting in intraluminal thrombus
2	Supply-demand	Mismatch due to, eg, ↑ ↑ or ↓↓ HR or BP, profound anemia or

	mismatch not due to Δ in CAD	hypoxemia, coronary vasospasm, HCM, severe AS
3	Sudden cardiac death	
4a	Related to PCI	Tn >5x 99th %ile or >20% rise if already elevated +≥1 MI clinical/imaging criteria above
4b	Stent thrombosis	
5	Related to CABG	Tn > 10x 99th %ile + new Qw or LBBB, angio confirmation, or new wall motion abnl

- Classification important as antithrombotic Rx relevant for type 1 but not type 2 MI, whereas anti-ischemic Rx (↑ O_2 supply & ↓ demand) particularly important for type 2

Early noninvasive imaging (also see noninvasive evaluation of CAD)

- If low prob of ACS (eg, ⊖ ECG & Tn) & stable → noninvasive fxnal or imaging test
- Treadmill electrocardiography: can be performed after 6-8 h of evaluation
- Radionuclide imaging in Pts who cannot exercise or have uninterpretable ECG
- Can perform acute rest perfusion imaging if ongoing or recent (w/in 2 h) pain (⊖ scan r/o ischemia; ⊕ scan could represent ischemia or infarct, need pain-free rest images)
- Echo (w/ or w/o stress) to assess for regional wall motion abnl; interpretation difficult in those w/ h/o prior MI
- Coronary CT angio (CCTA): NPV 98% for signif CAD, but PPV 35% for ACS; helpful to r/o CAD if low-intermed prob of ACS. CCTA vs noninvasive fxnal test for ischemia → ↓ time to dx & LOS, but ↑ probability of cath/PCI, contrast exposure & ↑ radiation (*NEJM* 2012;366:1393 & 367:299; *JACC* 2013;61:880)
- "Triple r/o" CT angiogram for CAD, PE, AoD

NONINVASIVE EVALUATION OF CAD

Stress testing (*Circ* 2007;115:1464; *JACC* 2012;60:1828)

- **Indications:** dx CAD, evaluate Δ in clinical status in Pt w/ known CAD, risk stratify s/p ACS, evaluate exercise tolerance, localize ischemia (imaging required)
- **Contraindications** (*Circ* 2002;106:1883; & 2012;126:2465)

  Absolute: AMI w/in 48 h, high-risk UA, acute PE, severe sx AS, uncontrolled HF, uncontrolled arrhythmias, myopericarditis, acute aortic dissection

  Relative: left main CAD, mod valvular stenosis, severe HTN, HCMP high-degree AVB, severe electrolyte abnl

Exercise tolerance test

- Generally preferred if patient can exercise to a meaningful level; Se ˜65%, Sp ˜80%
- Typically via treadmill

Protocol	Description
Standard Bruce	↑ speed & incline q3min until 85% max predicted HR or sxs
Modified Bruce	Adds two stages at start that require less work than standard Bruce stage 1; consider in sedentary/deconditioned Pt
Submaximal	Stop earlier (eg, 70% max predicted HR or 5 METs or any anginal sx); consider if recent MI

- Stationary cycle or arm ergometry (lower max workload) if Pt cannot walk
- Hold anti-ischemic meds (eg, nitrates, βB, CCB, ranolazine) if trying to dx obstructive CAD, but continue meds when assessing if Pt ischemic on current med regimen

Pharmacologic stress test (nb, requires imaging as ECG not interpretable)

- Use if unable to exercise, low exerercise tolerance, or recent MI. Se & Sp ≈ exercise.
- Preferred if LBBB or V-paced, as higher prob of false ⊕ exercise imaging (typically reversible or fixed anteroseptal defect).
- **Coronary vasodilator:** diffuse coronary arteriolar vasodilation → relative "coronary steal" from vessels w/ fixed epicardial disease. Reveals CAD, but *not* if Pt *ischemic* w/ *exercise.* Options include:

  Adenosine or dipyridamole (↑ adenosine reuptake). Side effects: flushing, bradycardia & AVB, dyspnea & bronchospasm.

  Selective A2A receptor agonist (eg, regadenoson): less flushing, dyspnea, bronchospasm

  Longer half-life of dipyridamole & regadenoson allow to be combined w/ exercise

  Avoid caffeine (adenosine receptor antagonist) w/in 12 h of test. Conversely, can use aminophylline to reverse effects of these agents.

  Contraindic: HoTN, sick sinus, high-degree AVB, bronchospasm (selective agents safer)
- **Chronotropes/inotropes** (more physiologic): dobutamine (may precip tachyarrhythmia)

Imaging for stress test (see Photo Inserts)

- Use if uninterpretable ECG (V-paced, LBBB, resting ST ↑ >1 mm, digoxin, LVH, WPW), after indeterminate ECG test, or if pharmacologic test
- Use when need to localize ischemia (often used if prior coronary revasc)
- Ideally use exercise as stress modality rather than pharmacologic
- **Radionuclide myocardial perfusion imaging** w/ images obtained at rest & w/ stress

  SPECT (eg, ^{99m}Tc-sestamibi): Se ~85%, Sp ~80%

  PET (rubidium-82): Se ~90%, Sp ~85%

ECG-gated imaging allows assessment of LV fxn (including regional systolic wall thickening or lack thereof as a sign of ischemia/infarction)

- **Echo** (exercise or dobuta): Se ~85%, Sp ~85%; no radiation; operator dependent
- Cardiac MRI (w/ pharmacologic stress) another option with excellent Se & Sp

Test results

- **HR** (must achieve ≥85% of max pred HR [220 - age] for *exer.* test to be dx), **BP** response, peak **double product** (HR × BP; nl >20k), HR recovery (HR_{peak} - $HR_{1\ min\ later}$; nl > 12)
- **Max exercise capacity** achieved (METS or min)
- Occurrence of **symptoms** (at what level of exertion and similarity to presenting sx)
- **ECG Δs:** *downsloping* or *horizontal* ST ↓ (≥1 mm) 80 ms after QRS predictive of CAD upsloping ST ↓ w/ rapid return to baseline usually due to ↑ HR & atrial repol artifact lead V_5 most sensitive; Δs isolated to inferior leads may be artifact location of ST ↓ does *not* localize ischemic territory

  STE: highly predictive of CAD & localizes; in aVR suggests LM CAD; nonspecific if in leads w/ prior Qw
- **Duke treadmill score** = exercise min - (5 × max ST dev) - (4 × angina index) [angina index = 0 none, 1 nonlimiting sxs, 2 limiting sxs]

Category	CAD	1-y mort	5-y survival
Low risk (≥5)	60% w/o signif stenosis	<1%	97%
Moderate risk (-10 to 4)	31% w/ 3VD or LM	2-3%	90%
High risk (≤-11)	74% w/ 3VD or LM	≥5%	65%

- **Imaging:** radionuclide defects or echocardiographic regional wall motion abnormalities reversible defect = ischemia; fixed defect = infarct; transient isch dilation = severe CAD false ⊕: breast → ant "defect" and diaphragm → inf "defect" false ⊖ may be seen if balanced (eg, 3VD) ischemia (global ↓ perfusion w/o regional Δs)

High-risk test results

- ECG: ST ↓ ≥2 mm *or* ≥1 mm in stage 1 *or* in ≥5 leads *or* ≥5 min in recovery; STE; VT
- Physiologic: ↓ or fail to ↑ BP, <4 METS, angina during exercise, Duke score ≤ -11; ↓ EF
- Radionuclide: ≥1 lg or ≥2 mod. reversible defects, transient LV cavity dilation, ↑ lung uptake
- High-risk test has PPV ~50% for LM or 3VD, ∴ consider coronary angio

Myocardial viability (*Circ* 2008;117:103; *Eur Heart J* 2011;31:2984 & 2011;32:810)

- Viable myocardium = dysfxn at rest, but not scarred and has potential for recovery
- Goal: identify hibernating or stunned myocardium that could regain fxn after revasc

Viability Test	Sens	Spec	Mechanism
MRI	~85%	~75%	Assesses cellular integrity
PET	~90%	~65%	Assesses cell metabolism
Dobut stress echo	~80%	~80%	Assesses contractile reserve
Myocard contrast echo	~85%	~50%	Assesses cellular integrity
Thallium: rest-redistrib or stress-reinjection	~85%	~55%	Assesses cellular integrity (K^+ analogue taken up by Na/K-ATPase)
Technetium-MIBI	~85%	~65%	Assesses cellular integrity (requires intact mitochondria)

- However, in Pts w/ ↓ EF, presence of viability did not identify differential clinical benefit from CABG vs med Rx (*NEJM* 2011;364:1617)

Coronary CT angio (CCTA; *NEJM* 2008;359:2324; *Circ* 2010;121:2509)

- High NPV to r/o CAD, but low PPV
- In Pts presenting with CP, presence of plaque sensitive (100%) but not specific (54%) for ACS, ∴ NPV 100%, PPV 17% (*JACC* 2009;53:1642). CCTA vs noninvasive fxnal test for ischemia → ↓ time to dx & LOS, but ↑ probability of cath/PCI, contrast exposure & ↑ radiation (*NEJM* 2012;366:1393 & 367:299; *JACC* 2013;61:880).
- In sx outPt, CCTA vs fxnal testing led to more radiation, coronary angiography & revascularization, but no difference in clinical outcomes (PROMISE *NEJM* 2015;372:1291)
- CCTA images may be limited if: HR >60-70 bpm, irregular rhythm, calcium deposition or stents (may create artifact), inability to breath hold 5 sec, vessel diameter < 1.5 mm. Image quality best at slower & regular HR (? give βB if possible, goal HR 55-60).
- Useful for assessing patency of bypass grafts

MRI angiography (*Lancet* 2012;379:453)

- Unlike CCTA, does not require iodinated contrast, HR control or radiation exposure. Can also assess LV fxn, enhancement (early = microvasc obstruction; late = MI). Limitations: cost, operator-dependent, long duration, ↓ spatial resolution.
- In head-to-head comparisons, CMRI and CCTA appear to have grossly comparable sensitivity and specificity (*JACC* 2005;46:92; *Annals* 2006;145:207)

Coronary artery calcium score (*NEJM* 2012;366:294; *JAMA* 2012;308:788)

- Quantifies extent of calcium; thus *estimates* plaque burden (but *not* % coronary stenosis)
- Compared w/ CCTA, CAC score assessment requires lower radiation exposure (1-2 mSv)
- CAC sensitive (91%) but not specific (49%) for presence of CAD; high NPV to r/o CAD

CAC Score	Suggested plaque burden
0	No disease
1-99	Mild disease
100-399	Moderate disease
>400	Severe disease

- ? value as screening test to r/o CAD in sx Pt (CACS <100 → 3% probability of signif CAD; but interpretation affected by age, gender)
- May provide incremental value to clinical scores for risk stratification (*JAMA* 2004;291:210). ACC/AHA guidelines note CAC assessment is reasonable in asx Pts w/ intermed risk (10-20% 10-y Framingham risk; ? value if 6-10% 10-y risk) (*Circ* 2010;122:e584).

STABLE ISCHEMIC HEART DISEASE

Epidemiology is U.S. (*Circ* 2015;131:e29)

- Prevalence: 20-39 y: <1%; 40-59 y: 5-6%; 60-79 y: 21% in ♂ & 11% in ♀; ≥80 y: 35% in ♂ & 19% in ♀; lifetime risk after age 40: 50% in men & 32% in women
- Ischemic heart disease (IHD) remains leading cause of death in both men & women

Workup (*Circ* 2012;126:e354)

- Initiate workup if suspected new dx of IHD or Δ in clinical status
- H&P, ECG (looking for ischemic or prior infarct Δs such as Qw, PRWP, ST or Tw abnl)

Pretest Likelihood of CAD (%) (*NEJM* 1979;300:1350; *Annals* 1993;118:81)

	Nonanginal (≤1 sx)		Atypical angina (2 sx)		Typical angina (all 3 sx)	
Age	Men	Women	Men	Women	Men	Women
35	3↔ 35	1 ↔ 19	8 ↔ 59	2 ↔ 39	30 ↔ 88	10 ↔ 78

45	9 ↔ 47	2 ↔ 22	21 ↔ 70	5 ↔ 43	51 ↔ 92	20 ↔ 79
55	23 ↔ 59	4 ↔ 21	45 ↔ 79	10 ↔ 47	80 ↔ 95	38 ↔ 82
65	49 ↔ 69	9 ↔ 29	71 ↔ 86	20 ↔ 51	93 ↔ 97	56 ↔ 84

Classic angina sx: substernal chest pain, provoked by exertion, relieved by rest or NTG. W/in each cell, 1st # is % for Pt w/o risk factors; 2nd is for Pt w/ DM, smoking, & hyperchol.

- **Noninvasive testing** (qv) if intermediate risk (ie, >10-20% & <80-90%). If Pt has low prob, then ↑ risk false ⊕; if very high prob, ⊖ test does not adeq r/o CAD, ∴ consider cor angio.
- **Coronary angio** if: high-risk noninv results (qv); very high pretest prob; refract angina; uncertain dx after noninvasive testing (& compelling need to determine dx), occupational need for definitive dx (eg, pilot) or inability to undergo noninvasive testing; survivor of SCD or life-threatening vent. arrhythmia; unexplained heart failure or ↓ EF; suspected spasm or nonatherosclerotic cause of ischemia (eg, anomalous coronary)

Optimal medical therapy (OMT) (*Circ* 2012;126:e354 & 2014;130:1749; HTN 2015;65:1372)

- **ASA** 75-162 βg/d; **βB** for 3 y post MI or if ↓ EF; **statin** (typically high intensity; see "Lipids")
- **ACEI** (or ARB) if HTN, DM, CKD or ↓ EF
- Risk factor targets: BP <140/90 (consider <130/80 if prior MI), Hb_{A1c} 7-9% (<7% if long life expect.), BMI 18.5-24.9 kg/m^2
- Smoking cessation; influenza vaccine
- Diet: ↑ veg, fruits, whole grains; ↓ sweets, sugar-sweetened bevs & red meat; sat fat 5-6% total cals, *trans* fat <1% total cals, chol <200 mg/d; Na ≤2400 mg/d (ideally ≤1500 mg/d)
- Exercise: ˜40 min moderate-to-vigorous physical activity 3-4x/wk

Medical therapies for symptomatic relief (*Circ* 2012;126:e354)

- **Beta blockers** 1st-line therapy
- **CCB** (verap/dilt or long-acting dihydro) or **long-acting nitrates:** add-on or if βB intolerant
- **Ranolazine** (↓ late inward Na+ current to ↓ myocardial demand): add-on or if βB intolerant

Coronary revascularization (*Circ* 2011;124:e574)

- If unacceptable angina despite max tolerated med Rx or if potential to improve survival
- OMT should be initial focus if stable & w/o critical anatomy & w/ normal EF
- Older studies showed survival benefit w/ revasc (CABG) vs med Rx (pre-statin era) if:

  LM (≥50% stenosis), 3VD (≥70% stenoses) espec if ↑ EF, 2VD w/ critical prox LAD, ? 1-2 VD w/ large area of viable, ischemic myocardium

Recent Studies of Revascularization in Modern Era of OMT

Compare	Trial	Pts	Result
PCI vs OMT	COURAGE[a]	1-3VD, EF >30%	PCI does *not* ↓ D/MI; faster sx resolution
	FAME-II[b]	≥1VD w/ FFR (qv) ≤0.8	PCI ↑ peri-PCI MI, but then 44% ↓ death/spont MI; ? greater benefit if FFR <0.65
CABG vs OMT	STITCH[c]	EF ≤35% (majority w/ 3VD)	CABG 20% ↓ CV death, no Δ in all-cause mortality
CABG vs PCI	SYNTAX[d]	3VD or LM	CABG ↓ D/MI & revasc but ± ↑ stroke High SYNTAX/SYNTAX II score[g] ID's those who benefit most from CABG
	PRECOMBAT[e]	LM	PCI ? noninferior but ↑ repeat revasc
	FREEDOM[f]	DM w/ ≥2VD	CABG ↓ D/MI, but ↑ stroke

[a] *NEJM* 2007;356:1503;

[b] *NEJM* 2014;371:1208;

[c] *NEJM* 2011;364:1607;

[d] *Lancet* 2013;381:629 & 639;

[e] *NEJM* 2011;364:1718;

[f] *NEJM* 2012;367:2375;

[g] www.syntaxscore.com

- LM or 3VD: CABG, espec if ↑ EF or DM; consider PCI if SYNTAX score ≤22 & high surg risk
- 2VD w/ prox LAD, ↓ EF, or extensive ischemia: CABG (espec if DM) or ? PCI
- ? 1VD (low FFR) w/ prox LAD + either ↓ EF or extensive ischemia: PCI or CABG (w/ LIMA)
- Exp't device to narrow coronary sinus ↓ angina (*NEJM* 2015;372:517)

LIPID DISORDERS

Measurements

- Lipoproteins = lipids (cholesteryl esters & triglycerides) + phospholipids + proteins include: chylomicrons, VLDL, IDL, LDL, HDL, Lp(a)
- Measure after 12-h fast; LDL is typically calculated w/ Friedewald equation:

  LDL-C = TC - HDL-C - (TG/5) [last term assumes TG:VLDL ratio = 5:1]; underestim. if TG >400 or LDL-C <70 mg/dL (*JAMA* 2013;310:2061); ∴ directly measure LDL-C

  Non-HDL-C (TC - HDL-C) and apoB are alternative nonfasting measures of risk

  Lipid levels stable up to 24 h after ACS and other acute illnesses, then ↓ and may take 6 wk to return to nl
- Metabolic syndrome (≥3 of following): waist ≥40" (♂) or ≥35" (♀); TG ≤150; HDL <40 mg/dL (♂) or <50 mg/dL (♀); BP ≤130/85 mmHg; fasting glc ≤100 mg/dL (*Circ* 2009;120:1640)
- Lp(a) = LDL particle bound to apo(a) via apoB; genetic variants a/w MI (*NEJM* 2009;361:2518)

Primary dyslipidemias

- Familial hypercholesterolemia (FH, 1:500): defective LDL receptor; ↑ ↑ chol, nl TG; ↑ CAD
- Familial defective apoB100 (1:1000): similar to FH
- Familial combined hyperlipidemia (1:200): polygenic; ↑ chol, ↑ TG, ↓ HDL; ↑ CAD
- Familial dysbetalipoproteinemia (1:10,000): ↑ chol & TG; xanthomas; ↑ CAD
- Familial hypertriglyceridemia (FHTG, 1:500): ↑ TG, ± ↑ chol, ↓ HDL, pancreatitis

Secondary Dyslipidemias

Category	Disorders
Endocrinopathies	Type 2 diabetes (↑ TG, ↓ HDL); lipodystrophy (↑ TG) Hypothyroidism (↑ LDL, ↑ TG); hyperthyroidism (↓ LDL) Cushing's syndrome & exogenous steroids (↑ LDL, ↑ TG)
Renal diseases	Renal failure (↑ LDL, ↑ TG); nephrotic syndrome (↑ LDL, ↑ TG)
Hepatic diseases	Cholestasis, PBC (↑ LDL); liver failure (↓ LDL); acute hepatitis (↑ TG)
Lifestyle	Obesity, sat & trans fat (↑ TG, ↓ HDL, ↑ LDL); sedentary lifestyle (↓ HDL); alcohol (↑ TG, ↑ HDL); tobacco (↓ HDL); anorexia (↑ LDL); very low-fat diet, high-refined-carb diet (↑ TG); preg (↑ LDL; ↑ TG)
Medications	Thiazides (↑ LDL, ↑ TG); βB (except carvedilol, ↑ TG, ↓ HDL); protease inhib (↑ TG); estrogens (↑ TG, ↑ HDL); androgens (↓ HDL); cyclosporine, amiodarone (↑ LDL); bile acid sequestrants, protease inhib, retin. acid, sirolimus, raloxifene, tamoxifen (↑ TG)

Physical exam findings

- Tendon xanthomas: seen on Achilles, elbows and hands; implies LDL >300 mg/dL
- Eruptive xanthomas: pimple-like lesions on extensor surfaces; implies TG >1000 mg/dL
- Xanthelasma: yellowish streaks on eyelids seen in various dyslipidemias
- Corneal arcus: common in older adults, imply hyperlipidemia in young Pts

Drug Treatment

Drug	↓ LDL	↑ HDL	↓ TG	Side effects/comments
Statins	20-60%	5-10%	10-25%	Doubling of dose → 6% further ↓ LDL. ↑ ALT in 0.5-3% (dose-dependent); ✓ before starting and then after as clinically indicated Myalgias <10% (not always ↑ CK), myositis 0.5%, rhabdo <0.1%, risk dose-dependent ↑ risk of DM (may be related to LDL-R; *JAMA* 2015;313:1029); screen if risk factors
Ezetimibe	15-20%	—	—	Well tolerated; typically w/ statin
Fibrates	5-15%	5-15%	35-50%	Myopathy risk ↑ w/ statin (gemfibrozil > fenofibrate). Dyspepsia, gallstones, ↑ Cr. ✓ renal fxn at baseline, 3 mo, q6mo.
Niacin	10-25%	~30%	40%	Flushing (less w/ sustained release; ASA preRx may ↓), hyperglycemia, ↑ UA. ✓ renal fxn, UA, glc ± HbA1c at baseline and q6mo or w/ uptitration.
Resins	20%	3-5%	↑	Bloating, binds other meds
Ω-3 FA	5% ↑	3%	25-50%	Dyspepsia, diarrhea, skin Δs, bleeding
PCSK9 inhibitors	40-65%	5-10%	15-25%	mAb inj SC q2w or q4w (*Lancet* 2012;380:2007 & *JACC* 2015;65:2638)
CETP inhibitors	~30%	140%	5-10%	*Investigational* (*NEJM* 2010;363:2406; *Lancet* 2015;386:452)

Treatment of LDL-C (*Lancet* 2014;384:607)

- **Statins:** every 1 mmol (39 mg/dL) ↓ LDL-C → 22% ↓ major vascular events (CV death, MI, stroke, revasc) in individuals w/ & w/o CAD (*Lancet* 2010;376:1670); ∴ *mainstay of therapy as potent, safe and well-tolerated*

- Consistent CV benefit even in individuals starting w/ LDL-C ≤60 mg/dL (*JACC* 2011;57:1666)
- No clear evidence to date to suggest any harm from achieving very low LDL-C levels
- Elevated hs-CRP *may* identify Pts who derive ↑ benefit (*NEJM* 2001;344:1959 & 2008;359:2195)
- Similar clinical benefit also seen w/ some older nonstatin Rxs (resins, fibrates, niacin) when sufficiently lowered LDL-C (*JACC* 2005;46:1855)
- **Ezetimibe:** ↓ major vascular events incl MI & stroke when added to statin post-ACS, w/ magnitude of benefit consistent w/ LDL-statin relationship (IMPROVE-IT, *NEJM* 2015;372:2387)
- **PCSK9 inhibitors:** ˜60% ↓ LDL on top of statin, as monoRx, and in FH (*EHJ* 2014;35:2249); prelim data w/ encouraging ↓ CV outcomes (*NEJM* 2015;372:1500), definitive trials ongoing

Treatment of HDL-C (*Lancet* 2014;384:618)

- Low levels of HDL-C associated with ↑ risk of MI
- However, Mendelian randomization studies do not support causal role (*Lancet* 2011;380:572)
- **Niacin:** in Pts w/ well-controlled LDL-C (<80 mg/dL) on a statin, minimally ↓ LDL, modestly ↑ HDL, and did not ↑ CV events (*NEJM* 2011;365:2255 & 2014;371:203)
- **CETP inhibitors:** one that ↑ HDL-C by 25% did not lead to clinical benefit in Pts w/ well-controlled LDL-C on a statin (*NEJM* 2012;367:2089); CV outcomes trials of inhibitors that ↑ HDL-C by 140% *and* ↑ LDL-C by ˜30% ongoing (*NEJM* 2010;363:2406; *JAMA* 2011;306:2099)

Treatment of hypertriglyceridemia (*Lancet* 2014;384:626)

- Reasonable to treat very high levels (>500- 1000 mg/dL) to ↓ risk of pancreatitis
- High levels of TG associated with ↑ risk of MI, but whether causal remains debated
- **Fibrates** (gemfibrozil & fenofibrate): mixed data in terms of ↑ vascular events, ? greater benefit if high TG (*Circ* 1992;85:37; *NEJM* 1999;341:410; *Lancet* 2005;366:1849; *NEJM* 2010;362:1563)
- **Fish oil** (containing Ω-3 fatty acids EPA & DHA): recent meta-analyses suggest supplementation w/o meaningful effect on CV events (*JAMA* 2012;308:1024)
- APOC3 inhibitors under study and ↑ TG by up to ˜70% (*NEJM* 2015;373:438)

Treatment of Lp(a)

- Consider ↓ to <50 mg/dL w/ niacin in intermed- to high-risk Pts (*EHJ* 2010;31:2844-53); however, benefit unclear espec if LDL-C well controlled (*JACC* 2014;63:520)

Guidelines (*Circ* 2014;129(Suppl 2):S1)

- Focus now on statin strategies, rather than achieving LDL-C goals
- Clinical atherosclerotic CV disease (ASCVD) includes h/o ACS, stable angina, arterial revasc, stroke, TIA, or PAD presumed to be of atherosclerotic origin
- 10-y CV Risk Score for CHD or stroke based on age, sex, race, SBP, TC, LDL, DM, tobacco, BP Rx; http://my.americanheart.org/cvriskcalculator
- Additional risk factors to consider include: LDL-C ≥160 mg/dL, genetic hyperlipid., FHx premature ASCVD, hsCRP >2 mg/L, CAC score ≥300 or ≥75th %ile, ABI <0.9.

2013 ACC/AHA Guideline of Treatment of Blood Cholesterol

Population	10-y CV risk	Statin Recommendation
Clinical ASCVD (ie, 2° prevention)	n/a	High intensity. If age >75 y, eval risk-benefit for high vs moderate intensity
LDL-C ≥190 mg/dL	n/a	High intensity
DM (type 1 or 2); age 40-75 y	≥7.5%	High intensity
	<7.5%	Moderate intensity
Age 40-75 y (and none of the above)	≥7.5%	High or moderate intensity
	5-<7.5%	Reasonable to offer moderate intensity
	<5%	Consider statin if additional risk factor

- If statin intolerant or LDL-C remains elevated despite high-intensity statin (as well as reinforcement of med adherence, lifestyle changes and exclusion of 2° causes of dyslipidemia) nonstatin LDL-lowering therapies remain reasonable
- If Pt does not tolerate high-intensity statin, consider dose reduction before d/c statin

Statin Doses & LDL-C Reduction

Intensity	↓ LDL-C	Rosuva	Atorva	Simva	Prava	Lova	Fluva	Pitava
High	≥50%	20-40	40-80	(80)				
Mod	30-50%	5-10	10-20	20-40	40-80	40	80	2-4
Low	<30%			10	10-20	20	20-40	1

Doses are in mg. Simva 80 mg has ↑ myopathy risk and should not be used unless dose already tolerated >12 mo.

ANGIOGRAPHY, PCI, & CABG

Precath checklist

- Document peripheral arterial exam (radial, femoral, DP, PT pulses; bruits); if plan for radial artery access, ✓ palmar arch intact (eg, w/ pulse oximetry & plethysmography), although value remains unproven (*JACC* 2014;63:1833)
- Ensure Pt can lie flat for several hours
- ✓ CBC, PT-INR (ideally ≤1.5), & Cr; blood bank sample
- NPO >6 h; IVF if appropriate (± bicarb; acetylcysteine no longer rec; see "CIAKI")

Vascular access

- Femoral artery commonly used; high puncture ↑ risk of retroperitoneal bleed; low puncture ↑ risk of peripheral arterial complic.; can access a synthetic graft if a few months old
- Radial artery: 33% ↓ major bleeding, trend to 15% ↓ in MACE & 28% ↓ mortality, espec if >80% of cases at center done radially (*Lancet* 2015;385:2465)

Periprocedural pharmacotherapy for PCI

- **Aspirin:** 325 mg × 1 (≥2 h prior to angio) → 81 mg qd
- **$P2Y_{12}$ inhibitor** *(choose one):*

  clopidogrel: 600 mg × 1 → 75 mg qd; preRx ↓ MACE (*JAMA* 2005;294:1224 & 2012;308:2507) prasugrel or ticagrelor (only in ACS, qv)

  cangrelor (IV, short-acting): ↓ early ischemic events vs clopi given w/o preload (*NEJM* 2013;368:1303)
- **GP IIb/IIIa inhibitor:** *consider adding* abciximab, eptifibatide, or tirofiban; data showing ↓ MACE largely before routine $P2Y_{12}$ inhibition and w/ UFH as anticoagulant. Remains reasonable espec if using clopidogrel and did not preRx.
- **Anticoagulant** *(choose one; typically* d/c'd *at end of* PCI*):*

  UFH: most common choice in U.S.

  bivalirudin: ↓ bleeding (espec vs UFH + GP IIb/IIIa inhib; *JAMA* 2015;313:1336), ± ↑ MI, ↑ stent thrombosis in STEMI (not mitigated by longer infusion), ↑ mortality in some but not all trials (*Lancet* 2014;384:599; MATRIX *NEJM* 2015); use if Pt has HIT enoxaparin (nb, cannot ✓ degree of anticoag)
- **Statin** (high-dose): PreRx ↓ peri-PCI myonecrosis (*Circ* 2011;123:1622) & ↓ risk of contrast-induced nephropathy (*JACC* 2014;63:71)

PCI options

- **Balloon angioplasty (POBA):** effective, but c/b dissection & elastic recoil & neointimal hyperplasia → restenosis; now reserved for small lesions & ? some SVG lesions
- **Bare metal stents (BMS):** ↓ elastic recoil → 33-50% ↓ restenosis & repeat revasc (to ˜10% by 1 y) c/w POBA; requires $P2Y_{12}$ inhibitor ≥4 weeks (ideally up to 6 mo)
- **Drug-eluting stents (DES)**

antiproliferative drug released over several weeks → ↓ neointimal hyperplasia ~75% ↓ restenosis, ~50% ↓ repeat revasc (to <5% by 1 y), no Δ D/MI (*NEJM* 2013;368:254)

delayed re-endothelialization & potentially proinflammatory polymers may cause ↑ in risk of late stent thrombosis; requires $P2Y_{12}$ inhibitor ≥6 mo

next generation DES (eg, w/ everolimus) w/ *lower* risk of stent thrombosis vs BMS (*Lancet* 2012;379:1393)

Other peri-PCI interventions

- **Fractional flow reserve (FFR):** ratio of max flow (induced by IV or IC adenosine) distal vs proximal to a stenosis; if used to guide PCI (ie, revasc only if FFR <0.8) → ↓ # stents & ↓ D/MI/revasc (*NEJM* 2009;360:213)
- Thrombus aspiration: small study showed manual aspiration of thrombus pre-PCI in STEMI ↓ mortality, but larger studies show no benefit and ↑ stroke (*Lancet* 2008;371:1915; *NEJM* 2013;369:1587 & 2015;372:1389)

Post-PCI complications

- Postprocedure ✓ vascular access site, distal pulses, ECG, CBC, Cr
- Vascular closure devices speed time to hemostasis and ↓ incidence of hematoma (*JAMA* 2014;312:1981)
- **Bleeding**

  hematoma/overt bleeding: **manual compression,** reverse/stop anticoag

  retroperitoneal bleed (if puncture above inguinal ligament)

  may p/w ↓ Hct ± flank or back pain; ↑ HR & ↓ BP late

  Dx w/ abd/pelvic CT (I^-)

  Rx: reverse/stop anticoag (d/w interventionalist), IV fluids/PRBC/plts as required; if bleeding uncontrolled, consult performing interventionalist or surgery

- **Vascular damage** (~1% of dx angio, ~5% of PCI; *Circ* 2007;115:2666)

  pseudoaneurysm: hematoma w/ continued communication to artery can present w/ triad of pain, expansile mass, systolic bruit; diagnose w/ U/S;

  Rx (if *pain* or >2 cm): U/S-directed thrombin injection (>95% success, depends on anatomy); surgical repair if very large or if minimally invasive Rx fails

  AV *fistula:* continuous bruit; Dx: U/S; Rx: surgical repair

  limb ischemia (emboli, dissection, clot): cool, mottled extremity, ↓ distal pulses; Dx: pulse volume recording (PVR), angio; Rx: percutaneous or surgical repair
- **Peri-PCI MI:** >5× ULN of Tn/CK-MB + either sx or ECG/angio/imaging Δs; Qw MI in <1%
- **Renal failure:** contrast-induced manifests w/in 24 h, peaks 3-5 d (see "CIAKI")
- **Cholesterol emboli syndrome**

  typically seen in middle-aged & elderly and w/ heavy burden of aortic atheroma multiple clinical manifestations (although may be delay between cath & s/s) including: intact distal pulses but livedo reticularis pattern and toe necrosis ("blue toe syndrome") renal failure: late and progressive (thus unlike CIAKI), ± eos in urine mesenteric ischemia: abd pain, GIB, pancreatitis

CNS: TIA, stroke, amaurosis fugax, Hollenhorst plaques (bright retinal lesion)

Dx: can only be confirmed by biopsy; may see ↑ circulating eos, ↓ complement, ↑ CRP, ↑ ESR, ↑ plts, ↑ fibrinogen

Rx: supportive; no clear benefit for anti-inflam or anticoagulant Rx

- **Stent thrombosis** (acute clot formation in stent): rare event, but high mortality can occur anytime between mins to yrs after PCI typically p/w ACS (often STEMI)

  typically due to either **mechanical problem** (stent underexpansion or unrecognized dissection, typically presents early) or **d/c of antiplt Rx** (espec if d/c both ASA & $P2Y_{12}$ inhib; *JAMA* 2005;293:2126)

- **In-stent restenosis** (neointimal hyperplasia): months after PCI, typically p/w gradual ↑ angina (10% p/w ACS). Due to combination of elastic recoil and neointimal hyperplasia; ↓ w/ DES vs BMS.

Duration of $P2Y_{12}$ inhibition

- In Pts w/ MI (qv), goal of antiplatelet therapy is ↑ CVD, MI, and stroke as well as rarer event of stent thrombosis. ∴ Long-term therapy *beyond* 12 mo is logical and has been shown to ↓ CV death, MI, and stroke (*NEJM* 2015;372:1791; *JACC* 2007;49:1982 & 2015;65:2211).
- In Pts w/ SIHD, concern for late (>30 d) stent thrombosis led to recs for 12-mo duration, but newer generation stents have lower risk of stent thrombosis
- Several small trials showed shorter duration of $P2Y_{12}$ inhibition (3-6 vs 12 mo) led to nonstatistically significant higher rates of MI and ST (but still infrequent) but less bleeding (*JACC* 2012;60:1340; *JAMA* 2013;310:2510; *EHJ* 2015;36:1252)
- Much larger DAPT trial showed that longer inhibition (30 vs 12 mo) led to 29% ↓ MACE and 71% ↓ ST (although rates and absolute risk reduction very low with newer generation stents), but ↑ bleeding and, in Pts w/ SIHD, marginally significant ↑ mortality (driven by non-CV mortality) (*NEJM* 2014;371:2155)

Need for premature discontinuation of antiplatelet therapy

- If possible, postpone major invasive procedures ≥1 mo after BMS or ≥3-6 mo after DES
- If not possible and high of risk bleeding during procedure, d/c prasugrel 7 d, clopidogrel 5 d, or ticagrelor 5 d (per prescribing information, but in major clinical trial, just ~3 d) prior to procedure. Continue ASA and resume $P2Y_{12}$ inhibitor w/ loading dose ASAP per surgery.
- If high-risk stent and bridging required, consider short-acting GP IIb/IIIa inhibitor (eptifi-batide or tirofiban) from 3 d until 4-6 h prior to surgery (*Circ* 2013;128:2785). Consider cangrelor (IV reversible $P2Y_{12}$ inhib) (*JAMA* 2012;307:265).

Advances in CABG technique

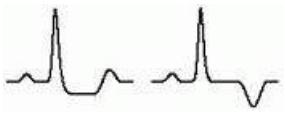
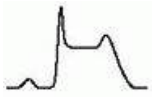
- **"Mini-CABG"** = minimally invasive. Thoracotomy or partial sternotomy rather than full sternotomy. Advantages include ↓ pain & ↓ LOS. May be on- or off-pump.
- **Off-pump** ("beating heart surgery"): avoids cardiopulmonary bypass but makes anastomotic suturing more challenging. In 1 study, ↑ CV death and ↓ graft patency at 12 mo c/w on-pump (*NEJM* 2009;361:1827); other studies w/ ≈ mortality w/ off- vs on-pump.
- **Robotic:** type of mini-CABG where endoscopic instruments inserted via small incisions to anastomose the

LIMA to the LAD on closed chest and beating heart

- **Hybrid procedures:** typically involves combo of LIMA-LAD mini-CABG with PCI of other vessels

ACUTE CORONARY SYNDROMES

Spectrum of Acute Coronary Syndromes

Dx	UA	NSTEMI	STEMI
Coronary thrombosis	Subtotal occlusion		Total occlusion
History	angina that is new-onset, crescendo or at rest; usually <30 min		angina at rest
ECG	± ST depression and/or TWI 		ST elevations 
Troponin/CK-MB	⊖	⊕	⊕⊕

Ddx (causes of myocardial ischemia/infarction other than atherosclerotic plaque rupture)

- **Nonatherosclerotic coronary artery disease**

  Spasm: Prinzmetal's variant, cocaine-induced (6% of CP + cocaine use r/i for MI)

  Dissection: spontaneous (vasculitis, CTD, pregnancy), aortic dissection with retrograde extension (usually involving RCA → IMI) or mechanical (catheter, surgery, trauma)

  Embolism (*Circ* 2015;132:241): AF, thrombus/myxoma, endocard., prosth valve; thrombosis

  Vasculitis: Kawasaki syndrome, Takayasu arteritis, PAN, Churg-Strauss, SLE, RA

  Congenital: anomalous origin from aorta or PA (coronary compressed), myocardial bridge (intramural segment)

- **Ischemic imbalance not due to plaque rupture** ("type 2" MI): ↑ myocardial O_2 demand (eg, ↑ HR, anemia, AS) or ↑ supply (hypotension, severe anemia)
- **Direct myocardial injury:** myocarditis; Takotsubo/stress CMP; toxic CMP; cardiac contusion

Clinical manifestations (*JAMA* 2005;294:2623)

- **Typical angina:** retrosternal pressure/pain/tightness ± radiation to neck, jaw or arms precip. by exertion, relieved by rest or NTG; in ACS, new-onset, crescendo or at rest; see "Chest Pain" for likelihood ratios for different sx
- **Associated symptoms:** dyspnea, diaphoresis, N/V, palpitations or lightheadedness
- Many MIs (˜20% in older series) are initially unrecognized b/c silent or atypical sx

- Atypical sxs (incl N/V & epig pain) may be more common with inferior ischemia
- Women may have ↑ freq of atypical sx vs men

Physical exam

- Signs of ischemia: S4, new MR murmur 2° pap. muscle dysfxn, paradoxical S_2, diaphoresis
- Signs of heart failure: ↑ JVP, crackles in lung fields, ⊕ S_3, HoTN, cool extremities
- Signs of other vascular disease: asymmetric BP (aortic dissection or subclavian disease), carotid or femoral bruits, ↓ distal pulses

ECG

- ✓ w/in 10 min of presentation, q15-30min × 1 h if initial ECG non-dx, w/ any Δ in sx, and routinely at 6-12 h; compare w/ baseline
- Signs of ischemia (*JAMA* 1998;280:1256)

  STE: generally ≥1 mm in ≥2 contiguous leads (see "STEMI" for details) new or presumed new (ie, not known to be old) LBBB w/ compelling H&P

  STD ≥0.5 mm (⊕ LR 3-5), TWI ≥2 mm (⊕ LR 2-3), hyperacute Tw
- Qw or PRWP may suggest prior MI, ∴ higher pretest probability of CAD
- Dx of STEMI if old LBBB (Sgarbossa's criteria): ≥1 mm STE *concordant* w/ direction of QRS (Se 73%, Sp 92%), STD ≥1 mm V_1-V_3 (Se 25%, Sp 96%) or STE ≥5 mm *discordant* w/ QRS (Se 31%, Sp 92%)

Localization of MI

Anatomic area	ECG leads w/ STE	Coronary artery
Septal	V_1-V_2	Proximal LAD
Anterior	V_3-V_4	LAD
Apical	V_5-V_6	Distal LAD, LCx or RCA
Lateral	I, aVL	LCx
Inferior	II, III, aVF	RCA (˜85%), LCx (˜15%)
RV	V_1-V_2 & V_4R (most Se)	Proximal RCA
Posterior	ST *depression* V_1-V_3 (= STE V_7-V_9 posterior leads)	RCA or LCx

If ECG non-dx and suspicion high, consider addt'l lateral (posterior) leads (V_7-V_9) to further assess distal LCx/RCA territory. Check right-sided precordial leads in patients with IMI to help detect RV involvement

(STE in V_4R most Se). STE in III > STE in II and lack of STE in I or aVL suggest RCA rather than LCx culprit in IMI.

Cardiac biomarkers

- Troponin (Tn) preferred over CK-MB
- ✓ Tn at baseline & 3-6 h after sx onset; may also ✓ beyond 6 h if high index of suspicion based on clinical presentation or ECGs or if sx Δ
- Rise to >99th %ile in approp. clinical setting dx of MI (see "Chest Pain")
- In Pts w/ ACS & ↓ CrCl, ↓ Tn still portends poor prognosis (*NEJM* 2002;346:2047)

Other potential dx tests

- If low prob, **stress test, CT angio** or rest perfusion imaging to r/o CAD (see "Chest Pain")
- TTE (new wall motion abnl) suggestive of ACS but not specific, as may be seen if old MI
- Coronary angio gold standard for evaluation of CAD

Prinzmetal's (variant) angina

- Coronary spasm → transient STE usually w/o MI (*but* MI, AVB, VT can occur)
- Pts usually young, smokers, ± other vasospastic disorders (eg, migraines, Raynaud's)
- Most frequent between midnight and early morning when vagal tone is highest
- Provocation testing: spasm can be precipitated at angio w/ IC ergonovine or acetylchol. positive test = severe narrowing w/ sx or ECG Δs; nonobstructive CAD typically seen; rarely done as risks include refractory/recurrent spasm or arrhythmia
- Noninvasive testing: hyperventilation, 12-lead Holter, exercise study
- Treatment: often initiated empirically without provocation testing: high-dose CCB (dilt, verap or nifed all roughly ≈) & standing nitrates (+SL prn) ? α-blockers/statins; d/c smoking

  avoid high-dose ASA (can inhibit prostacyclin & worsen spasm), nonselect βB, triptans
- Cocaine-induced vasospasm: use CCB, nitrates, ASA; ? avoid βB, but data weak and labetalol appears safe (*Archives* 2010;170:874; *Circ* 2011;123:2022)

Likelihood of ACS

Feature	High (any of below)	Intermediate (no high features, any of below)	Low (no high/inter. features, may have below)
History	Chest or L arm pain like prior angina, h/o CAD (incl MI)	Chest or arm pain age >70 y, male, diabetes	Atypical sx (eg, pleuritic, sharp or positional pain)
Exam	HoTN, diaphoresis, HF,	PAD or cerebrovas-	Pain reproduced on palp.

	transient MR	cular dis.	
ECG	New STD (≥1 mm) TWI in mult leads	Old Qw, STD (0.5-0.9 mm), TWI (>1 mm)	TWF/TWI (<1 mm) in leads w/ dominant R wave
Biomarkers	⊕ Tn or CK-MB	Normal	Normal

(Adapted from ACC/AHA 2007 Guideline Update for UA/NSTEMI, *Circ* 2007;116:e148)

Approach to triage

- If hx and initial ECG & Tn non-dx, repeat ECG q15-30min × 1 h & Tn 3-6 h after sx onset
- If remain nl and low likelihood of ACS, search for alternative causes of chest pain
- If remain nl, have ruled out MI, *but* if suspicion for ACS based on hx, then still need to r/o UA w/ stress test to assess for inducible ischemia (or CTA to r/o CAD);

  if low risk (eg, age ≤70; ø prior CAD, CVD, PAD; ø rest angina) can do before d/c from ED or as outPt w/in 72 h (0% mortality, <0.5% MI, *Ann Emerg Med* 2006;47:427)

  if not low risk, admit and initiate Rx for possible ACS and consider stress test or cath

Acute Anti-Ischemic and Analgesic Treatment

Nitrates (SL or IV) 0.3-0.4 mg SL q5min ×3, then consider IV if still sx	Use for relief of sx, control HTN or Rx of HF No clear ↓ in mortality *Caution* if preload-sensitive (eg, HoTN, AS, sx RV infarct); contraindic if recent PDE5 inhibit use
β-blockers eg, metop 25-50 mg PO q6h titrate slowly to HR 50-60 IV only if HTN and no HF	↓ ischemia & progression of UA to MI (*JAMA* 1988;260:2259) STEMI: ˜20% ↓ arrhythmic death or reMI, but 30% ↑ cardiogenic shock early (espec if signs of HF), & ∴ no Δ overall mortality (*Lancet* 2005;366:1622) In Pts w/o HF, IV βB prior to 1° PCI ↓ infarct size and ↑ EF (*Circ* 2013;128:1495) *Contraindic.* PR >0.24 sec, HR <60, 2°/3° AVB, severe bron-chospasm, s/s HF or low output, risk factors for shock (eg, >70 y, HR >110, SBP <120, late presentation STEMI)
CCB (nondihydropyridines)	If cannot tolerate βB b/c bronchospasm; otherwise has similar contraindications as βB Rx
Morphine	Relieves pain, ↓ anxiety, venodilation → ↓ preload ∴ use for persistent sx or CHF. Do not mask refractory sx. May delay onset of antiplatelet Rx (*JACC* 2014;63:630)
Oxygen	Use prn for resp distress or to keep S_aO_2 >90% ? ↑ infarct size in STEMI w/o hypoxia (*Circ* 2015;131:2143)

Other early adjunctive therapy

- **High-intensity statin therapy** (eg, atorvastatin 80 mg qd) ↓ ischemic events w/ benefit emerging w/in wks (*JAMA* 2001;285:1711 & *JACC* 2005;46:1405) ↓ peri-PCI MI (*JACC* 2010;56:1099); ↓ contrast-induced nephropathy (*JACC* 2014;63:71)
- **ACEI/ARB:** start once hemodynamics and renal function stable Strong indication for ACEI if heart failure, EF <40%, HTN, DM, CKD; ˜10% ↑ mortality, greatest benefit in ant. STEMI or prior MI (*Lancet* 1994;343:1115 & 1995;345:669)

  Start w/ low dose of short-acting (eg, captopril 6.25 mg tid), titrate up as tolerated ARB appear ≈ ACEI (*NEJM* 2003;349:20); give if contraindic to ACEI
- Ezetimibe, aldosterone blockade, and ranolazine discussed later (long-term Rx)
- IABP: can be used for refractory angina when PCI not available

NSTE-ACS (*Circ* 2014;130:e344)

Key issues are antithrombotic regimen and invasive vs conservative strategy

Antiplatelet Therapy

Aspirin 162-325 mg × 1, then 81 mg qd (non-enteric coated, chewable)	50-70% ↓ D/MI (*NEJM* 1988;319:1105) Low dose (˜81 mg) pref long term (*NEJM* 2010;363:930) If allergy, use clopi and/or desensitize to ASA

$P2Y_{12}$ (ADP receptor) inhibitor (choose one of the following in addition to ASA). Timing remains controversial. Some data support benefit of clopidogrel preRx prior to angiography (*JAMA* 2012;308:2507). Ticagrelor was given upstream in pivotal study. Prasugrel should be given once PCI planned (ie, anatomy defined). European guidelines recommend $P2Y_{12}$ inhibitor as soon as possible after presentation (*EHJ* 2011;32:2999).

• **Ticagrelor** 180 mg × 1 → 90 mg bid Reversible binding, but wait 3-5 d prior to surg Use only with ASA <100 mg qd	Preferred over clopidogrel More rapid and potent plt inhib c/w clopi 16% ↓ CVD/MI/stroke & 21% ↓ CV death c/w clopi; ↑ non-CABG bleeding (*NEJM* 2009;361;1045) Sensation of dyspnea (S_aO_2 & PFTs nl) and ventricular pauses; perhaps b/c blocks adenosine reuptake
• **Prasugrel** 60 mg × 1 at PCI → 10 mg qd (consider 5 mg/d if <60 kg) Wait 7 d prior to surgery	Use at time of PCI; preferred over clopidogrel More rapid and potent plt inhib c/w clopi 19% ↓ CVD/MI/stroke in ACS w/ planned PCI vs clopi, but ↑ bleeding (*NEJM* 2007;359:2001), incl fatal bleeds Not sup to clopi if med mgmt w/o PCI (*NEJM* 2012;367:1297) In NSTE-ACS, should be given at time of PCI and not upstream due to ↑ bleeding (*NEJM* 2013;369:999) Contraindic. if h/o TIA/CVA; ? avoid if >75 y

• **Clopidogrel**[*] 300-600 mg × 1 → 75 mg qd Requires ˜6 h to steady state	ASA+clopi → 20% ↓ CVD/MI/stroke vs ASA alone ↑ benefit if given hrs *prior* to PCI, but then if require CABG, need to wait >5 d after d/c clopi
• **Cangrelor** Only IV $P2Y_{12}$ inhibitor Rapid onset/offset; t½ 3-5 min	22% ↓ CV events (mostly peri-PCI MI and stent thrombosis) vs clopi 300 mg at time of PCI; no significant ↑ bleeding (*NEJM* 2013;368:1303) Unclear benefit if upstream clopi (*NEJM* 2009;361:2318) and no data vs prasugrel or ticagrelor
GP IIb/IIIa inhibitors (GPI) Abciximab: LD 0.25 mg/kg IV, then 0.125 mcg/kg/min Eptifibatide: LD 180 mcg/kg IV ×2, then 2 mcg/kg/min (½ dose if CrCl <50 mL/min) Tirofiban: LD 25 mcg/kg IV, then 0.15 mcg/kg/min (½ dose if CrCl <30 mL/min)	No clear benefit for routinely starting prior to PCI and ↑ bleeding (*NEJM* 2009;360:2176). Consider epti or tiro if refractory ischemia despite optimal Rx while awaiting angio. Consider in high-risk Pts (eg, large thrombus burden) at time of PCI, espec if using clopi and not preRx'd. Often administered 18-24 h post PCI, but shorter duration (˜2 h) may be as efficacious and with ↓ bleeding (*JACC* 2009;53:837); D/C eptifibatide/tirofiban ≥2-4 h and abciximab ≥12 h prior to urgent CABG.

[*]Utility of platelet function testing remains unproven (*JAMA* 2011;305:1097; *NEJM* 2012;367:2100), but studies underpowered. ˜30% pop has ↓ fxn *CYP2C*19 allele → ↑ CV events if PCI on clopi compared w/ wild type (*NEJM* 2009;360:354; *JAMA* 2010;304:1821).

Anticoagulant Therapy (choose one)

UFH: 60 U/kg IVB (max 4000 U) then 12 U/kg/h (max 1000 U/h initially) × 48 h or until end of PCI	24% ↓ D/MI (*JAMA* 1996;276:811) Titrate to aPTT 1.5-2× control (˜50-70 sec) Hold until INR <2 if already on warfarin
Enoxaparin (low-molec-wt heparin) 1 mg/kg SC bid (± 30 mg IVB) (qd if CrCl <30) × 2-8 d or until PCI	˜10% ↓ D/MI vs UFH (*JAMA* 2004;292:45,89). Can perform PCI on enox (*Circ* 2001;103:658), but ↑ bleeding if switch b/w enox and UFH.
Bivalirudin (direct thrombin inhibitor) 0.75 mg/kg IVB at PCI → 1.75 mg/kg/h	↓ bleeding (espec vs UFH + GPI), ± ↑ early MI (*Lancet* 2014;384:599). Use instead of UFH if HIT.
Fondaparinux (Xa inhibitor) 2.5 mg SC qd × 2-8 d	C/w enox, 17% ↓ death & 38% ↓ bleeding (*NEJM* 2006;354:1464). However, ↑ risk of catheter thrombosis; ∴ must supplement w/ UFH if PCI.

Coronary angiography (*Circ* 2014;130:e344)

- **Immediate/urgent coronary angiography** (w/in 2 h) if refractory/recurrent angina or hemodynamic or

electrical instability

- **Invasive (INV) strategy =** routine angiography w/in 72 h (*NEJM* 2009;360:2165)

  Early (w/in 24 h) if: ⊕ Tn, ST Δ, GRACE risk score (www.outcomes-umassmed.org/grace) >140

  Delayed (ie, acceptable anytime w/in 72 h) if no indication for early/immediate cath but has other high-risk predictors incl: diabetes, EF <40%, GFR <60, post-MI angina , TIMI Risk Score ≥3, GRACE score 109-140, PCI w/in 6 mo, prior CABG

  Invasive strategy leads to 32% ↓ rehosp for ACS, nonsignif 16% ↓ MI, no Δ in mortality c/w cons. (*JAMA* 2008;300:71); ↑ peri-PCI MI counterbalanced by ↓ ↓ in spont. MI; mortality benefit seen in some studies, likely only if cons. strategy w/ low rate of angio

  ↑ risk of death or MI if invasive strategy deferred beyond 72 h (*JAMA* 2003;290:1593)

- **Conservative (CONS) strategy =** selective angio. Medical Rx with pre-d/c stress test; angio only if recurrent ischemia or ⊕ ETT. *Indicated for:* low TIMI Risk Score, Pt or physician preference in absence of high-risk features, low-risk women (*JAMA* 2008;300:71).

TIMI Risk Score (TRS) for UA/NSTEMI (*JAMA* 2000;284:835)

Calculation of Risk Score		Application of Risk Score	
Characteristic	**Point**	**Score**	**D/MI/UR by 14 d**
Historical		0-1	5%
Age ≥65 y	1	2	8%
≥3 Risk factors for CAD	1	3	13%
Known CAD (stenosis ≥50%)	1	4	20%
ASA use in past 7 d	1	5	26%
Presentation		6-7	41%
Severe angina (≥2 episodes w/in 24 h)	1	Higher risk Pts (TRS ≥3) derive ↑ benefit from LMWH, GP IIb/IIIa inhibitors and early angiography (*JACC* 2003;41:89S)	
ST deviation ≥0.5 mm	1		
⊕ cardiac marker (troponin, CK-MB)	1		

RISK SCORE = Total points **(0-7)**

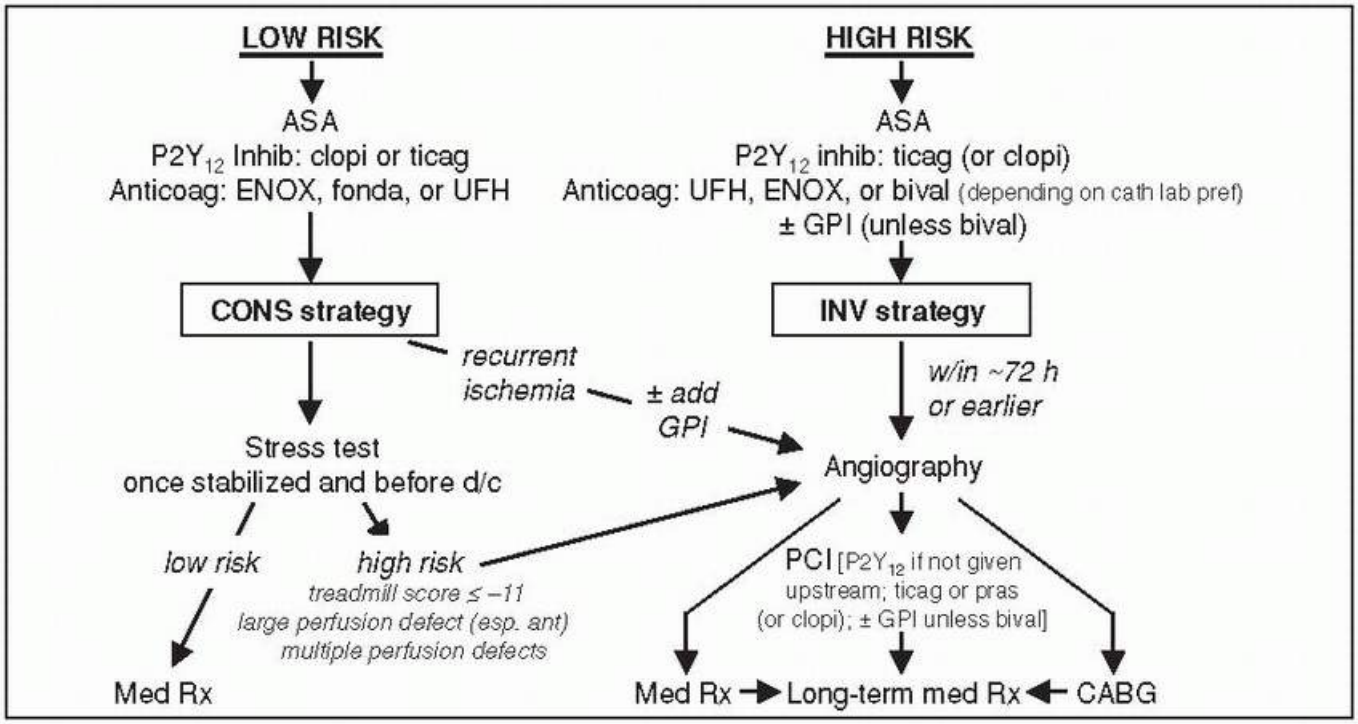


Figure 1-2 Approach to UA/NSTEMI

STEMI

Requisite STE (at J point)

- ≥2 contiguous leads w/ ≥1 mm (except for V_2-V_3: ≥2 mm in ♂ and ≥1.5 mm in ♀), or
- New or presumed new LBBB w/ compelling H&P, or
- True posterior MI: ST depression V_1-V_3 ± tall Rw w/ STE on posterior leads (V_7-V_9)

Reperfusion ("time is muscle")

- Immediate reperfusion (ie, opening occluded culprit coronary artery) is critical
- In PCI-capable hospital, goal should be **primary PCI w/in 90 min** of 1st medical contact
- In non-PCI-capable hospital, consider *transfer* to PCI-capable hospital (see below), o/w **fibrinolytic therapy** w/in 30 min of hospital presentation. If dx confirmed, administration of fibrinolytic in ambulance prior to arrival can be considered
- Do not let decision regarding *method* of reperfusion delay *time* to reperfusion

Primary PCI (*NEJM* 2007;356:47; *JACC* 2013;61:e78)

- Definition: immediate PCI upon arrival to hospital or transfer for immediate PCI
- Indications: STE + sx onset < 12 h; ongoing ischemia 12-24 h after sx onset; shock or severe HF regardless of time
- Superior to lysis: 27% ↓ death, 65% ↓ reMI, 54% ↓ stroke, 95% ↑ ICH (*Lancet* 2003;361:13)

- *Transfer* to center for 1° PCI superior to lysis (*NEJM* 2003;349:733). ∴ If initially seen at non-PCI capable hosp, transfer for PCI if door-in to door-out time can be ≤30 min and 1st medical contact to PCI time estimated to be ≤120 min.
- Thrombus aspiration: small study showed ↓ mortality, but larger studies show no benefit and ↑ stroke (*Lancet* 2008;371:1915; *NEJM* 2013;369:1587 & 2015;372:1389)
- Small studies have demonstrated ↓ MACE w/ complete revasc vs culprit artery alone (*NEJM* 2013; 369:1115; *JACC* 2015;65:963), large study ongoing; alternatively, could assess ischemia due to residual lesions w/ imaging stress (*Circ* 2011;124:e574)

Fibrinolysis vs Hospital Transfer for Primary PCI: Assess Time and Risk

1. **Time required for transport to skilled PCI lab:** door-to-balloon <120 min & [door-to-balloon]-[door-to-needle] <1 h favors transfer for PCI
2. **Risk from STEMI:** high-risk Pts (eg, shock) fare better with mechanical reperfusion
3. **Time to presentation:** efficacy of lytics ↓ w/ ↑ time from sx onset, espec >3 h
4. **Risk of fibrinolysis:** if high risk of ICH or bleeding, PCI safer option Adapted from ACC/AHA 2013 STEMI Guidelines (*Circ* 2013;127:529)

Fibrinolysis

- Indic: STE/LBBB + sx <12 h + >120 min before PCI can be performed; benefit if sx >12 h less clear; reasonable if persist. sx & STE or hemodyn instability or large territory at risk
- Fibrin-spec lytics (TNK, TPA, RPA) ↑ artery patency vs streptokinase (*JACC* 2013;61:e78)
- Mortality ↓ ~20% in anterior MI or LBBB and ~10% in IMI c/w ø reperfusion Rx
- Prehospital lysis (ie, ambulance): further 17% ↓ in mortality (*JAMA* 2000;283:2686)
- ~1% risk of ICH; high-risk groups include elderly (~2% if >75 y), women, low wt
- Although age not contraindic., ↑ risk of ICH in elderly (>75 y) makes PCI more attractive
- Successful reperfusion gauged by sx & ECG: sudden CP resolution & ≥70% resolution of STE indicative of successful reperfusion; conversely, STE resolution <50% after 60-90 min should prompt consideration of rescue PCI (qv)

Contraindications to Fibrinolysis

Absolute contraindications	Relative contraindications
• Any prior ICH • Intracranial neoplasm, aneurysm, AVM	• Hx of severe HTN or SBP >180 or DBP >110 on presentation (? absolute contra. if low-risk MI)

- Ischemic stroke w/in 3 mo (unless acute w/in 4.5 h) or closed head trauma w/in 3 mo
- Active internal bleeding or known bleeding diathesis
- Head/facial trauma w/in 3 mo
- Head/spinal surgery w/in 2 mo
- Suspected aortic dissection
- Severe uncontrollable HTN
- For SK, SK Rx w/in 6 mo
- Ischemic stroke >3 mo prior
- Dementia
- Recent traumatic or prolonged CPR >10 min
- Trauma or major surgery w/in 3 wk
- Recent internal bleed (w/in 2-4 wk); active PUD
- Noncompressible vascular punctures
- Prior SK exposure (if considering SK)
- Pregnancy
- Current use of anticoagulants

Nonprimary PCI

- Facilitated or pharmacoinvasive PCI = upstream lytic, GPI or GPI + ½ dose lytic before PCI; in general no clear clinical benefit & ↑ bleeding (*Lancet* 2006;367:569; *NEJM* 2013;368:1379)
- Rescue PCI if shock, unstable, failed reperfusion or persistent sx (*NEJM* 2005;353:2758)
- Routine angio ± PCI w/in 24 h of successful lysis: ↓ D/MI/revasc (*Lancet* 2004;364:1045) and w/in 6 h ↓ reMI, recurrent ischemia, & HF compared to w/in 2 wk (*NEJM* 2009;360:2705);

  ∴ *if lysed at non-PCI capable hospital, consider transfer to PCI-capable hospital ASAP espec if high-risk presentation (eg, anterior MI, inferior MI w/ low EF or RV infarct, extensive STE or LBBB, HF, ↓ BP or ↑ HR)*
- *Late* PCI (median day 8) of occluded infarct-related artery: no benefit (*NEJM* 2006;355:2395)

Antiplatelet Therapy

Aspirin 162-325 mg × 1 (crushed/chewed) then 81 mg qd	23% ↓ in death (*Lancet* 1988;ii:349) Should not be stopped if CABG required
P2Y$_{12}$ inhibitor Give ASAP (do not wait for angio) Ticagrelor or prasugrel (if PCI) as detailed above Clopidogrel: 600 mg pre-PCI; 300 mg if lysis (no LD if >75 y) → 75 mg qd	*Lysis:* clopidogrel 41% ↑ in patency, 7% ↓ mort, no Δ major bleed or ICH (*NEJM* 2005;352:1179; *Lancet* 2005;366:1607); no data for pras or ticag w/ lytic *PCI:* prasugrel and ticagrelor ↓ CV events c/w clopi (*Lancet* 2009;373:723 & *Circ* 2010;122:2131) *Nb, antiplt effects delayed in STEMI Pts*
GP IIb/IIIa inhibitors abciximab, eptifibatide, tirofiban	*Lysis:* no indication (*Lancet* 2001;357:1905) *Peri-PCI:* 60% ↓ D/MI/UR (*NEJM* 2001;344:1895)

Adapted from ACC/AHA 2013 STEMI Guidelines Update (*Circ* 2013;127:529); *Lancet* 2013;382:633

Anticoagulant Therapy (choose one)

UFH 60 U/kg IVB (max 4000	No demonstrated mortality benefit ↑ patency with fibrin-specific lytics

U) 12 U/kg/h (max 1000 U/h initially)	Titrate to aPTT 1.5-2× control (˜50-70 sec)
Enoxaparin *Lysis:* 30 mg IVB → 1 mg/kg SC bid (adjust for age >75 & CrCl) *PCI:* 0.5 mg/kg IVB	*Lysis:* 17% ↓ D/MI w/ ENOX × 7 d vs UFH × 2 d (*NEJM* 2006;354;1477) *PCI:* ↓ D/MI/revasc and ≈ bleeding vs UFH (*Lancet* 2011;378:693)
Bivalirudin 0.75 mg/kg IVB → 1.75 mg/kg/hr IV (ongoing research on prolonged infusions)	*PCI:* ↓ bleeding (espec vs UFH + GP IIb/IIIa inhib), ± ↑ MI, ↑ stent thromb (not mitigated by longer infusion), ↓ mortality in some but not all trials (*Lancet* 2014;384:599; *JAMA* 2015;313:1336; MATRIX NEJM 2015)
Fondaparinux 2.5 mg IVB → 2.5 mg SC qd Contraindic if CrCl ≤30 mL/min	*Lysis:* superior to placebo & to UFH, with less bleeding (*JAMA* 2006;295;1519) *PCI:* risk of catheter thromb.; should not be used

Adapted from ACC/AHA 2013 STEMI Guidelines (*Circ* 2013;127:529); *Lancet* 2013;382:633

Intraaortic Balloon Pump (IABP) Counterpulsation

- Inflates during diastole and deflates during systole to ↑ coronary flow and ↑ afterload
- *Routine* use in high-risk STEMI → ↑ stroke/bleeds w/o Δ in survival, infarct size or EF (*EHJ* 2009;30:459; *JAMA* 2011;306:1329)
- In cardiogenic shock, no survival benefit w/ IABP if early revasc (*NEJM* 2012;367:1287); 18% ↓ death in Pts w/ cardiogenic shock treated with lytic (*EHJ* 2009;30:459)

LV failure (˜25%)

- Diurese to achieve PCWP 15-20 → ↑ pulmonary edema, ↓ myocardial O_2 demand
- ↓ Afterload → ↑ stroke volume & CO, ↓ myocardial O_2 demand can use IV NTG or nitroprusside (risk of coronary steal) → short-acting ACEI
- Inotropes if HF despite diuresis & ↓ afterload; use dopamine, dobutamine or milrinone
- **Cardiogenic shock** (˜7%) = MAP < 60 mmHg, CI <2 L/min/m^2, PCWP >18 mmHg; inotropes, mech support [eg, VAD, IABP (see above)] to keep CI >2; pressors to keep MAP >60; if not done already, coronary revasc (*NEJM* 1999;341:625)

IMI complications (*Circ* 1990;81:401; *NEJM* 1994;330:1211; *JACC* 2003;41:1273)

- **Heart block** (˜20%, occurs because RCA typically supplies AV node) 40% on present., 20% w/in 24 h, rest by 72 h; high-grade AVB can develop abruptly Rx: atropine, epi, aminophylline (100 mg/min × 2.5 min), temp pacing wire
- **RV infarct** (proximal RCA occlusion → compromised flow to RV marginal branch) Angiographically in 30-50%, but only ½ of those clinically signif. HoTN; ↑ JVP, ⊕ Kussmaul's; 1 mm STE in V_4R; RA/PCWP ≥0.8;

RV dysfxn on TTE

Rx: optimize preload (RA goal 10-14, *BHJ* 1990;63:98); ↑ contractility (dobutamine); maintain AV synchrony (pacing as necessary); reperfusion (*NEJM* 1998;338:933); mechanical support (IABP or RVAD); pulmonary vasodilators (eg, inhaled NO)

Mechanical complications (incid. <1% for each; typically occur a few days post-MI)

- **Free wall rupture:** ↑ risk w/ lysis, large MI, ↑ age, ♀, HTN; p/w PEA or hypoTN, pericardial sx, tamponade; Rx: volume resusc., ? pericardiocentesis, inotropes, **surgery**
- **VSD:** large MI in elderly; AMI → apical VSD, IMI → basal septum; 90% w/ harsh murmur ± thrill (*NEJM* 2002;347:1426); Rx: diuretics, vasodil., inotropes, IABP, **surgery,** perc. closure
- **Papillary muscle rupture:** more common after inf MI (PM pap. muscle supplied by PDA alone) than ant MI (AL pap. muscle supplied by diags & OMs); 50% w/ new murmur, rarely a thrill, → *v* wave in PCWP tracing; asymmetric pulmonary edema on CXR (often worse in RUL due to direction of jet). Rx: diuretics, vasodilators, IABP, **surgery.**

Arrhythmias post-MI

- Treat as per ACLS for unstable or symptomatic bradycardias & tachycardias
- **AF** (10-16% incidence): βB or amio, ± digoxin (particularly if HF), heparin
- **VT/VF:** lido or amio × 6-24 h, then reassess; ↑ βB as tol., replete K & Mg, r/o ischemia; early monomorphic (<48 h post-MI) does *not* carry bad prognosis. Beyond 48 h, VT/VF a/w worse prognosis → consider wearable defibrillator (qv).
- Accelerated idioventricular rhythm (AIVR): slow VT (<100 bpm), often seen after successful reperfusion; typically self-terminates and does not require treatment
- May consider ***backup* transcutaneous pacing** (TP) if: 2° AVB type I, BBB
- **Backup TP *or* initiate transvenous pacing** if: 2° AVB type II; BBB + AVB
- **Transvenous pacing** (TV) if: 3° AVB; new BBB + 2° AVB type II; alternating LBBB/RBBB (can bridge w/ TP until TV, which is best accomplished under fluoroscopic guidance)

Other Post-MI Complications

Complication	Clinical features	Treatment
LV thrombus	~30% incid. (espec lg antero-apical MI)	Anticoagulate × 3-6 mo
Ventricular aneurysm	Noncontractile outpouching of LV; 8-15% incid. (espec ant); persist STE	Surgery or perc repair if HF, thromboemboli, arrhythmia

Ventricular pseudoaneurysm	Rupture → sealed by thrombus and pericardium (espec in inf). Typically w/ narrow neck as c/w true aneurysm; Dx w/ cardiac MRI, CTA, or TEE.	Urgent surgery (or percutaneous repair)
Pericarditis	10-20% incid.; 1-4 d post-MI ⊕ pericardial rub; ECG Δs rare	High-dose ASA > aceta., colchicine, narcotics; minimize anticoag
Dressler's syndrome	<4% incid.; 2-10 wk post-MI fever, pericarditis, pleuritis	High-dose aspirin, NSAIDs

Prognosis

- In registries, in-hospital mortality is 6% w/ reperfusion Rx (lytic or PCI) and ~20% w/o
- Predictors of mortality: age, time to Rx, anterior MI or LBBB, heart failure (*Circ* 2000;102:2031)

Killip Class

Class	Definition	Mort.
I	no CHF	6%
II	⊕ S3 and/or basilar rales	17%
III	pulmonary edema	30-40%
IV	cardiogenic shock	60-80%

(*Am J Cardiol* 1967;20:457)

Forrester Class Mortality

		PCWP (mmHg)	
		<18	>18
CI	>2.2	3%	9%
	≤2.2	23%	51%

(*NEJM* 1976;295:1356)

TIMI Risk Score for STEMI

Characteristic	Points	Characteristic (cont)	Points	Score	30-d death
Age 65-74/≥75 y	2/3	Ant MI or new LBBB	1	0-2	˜1-2%
SBP <100 mmHg	3	h/o DM, HTN or angina	1	3-4	˜4-6%
HR >100 bpm	2	Wt <67 kg	1	5-6	˜10-15%
Killip class II-IV	2	Time to Rx >4 h	1	≥7	≥20%

(*JAMA* 2001;286:1356)

PREDISCHARGE CHECKLIST AND LONG-TERM POST-ACS MANAGEMENT

Risk stratification

- Stress test if anatomy undefined; consider stress if signif residual CAD post-PCI of culprit
- Assess LVEF prior to d/c; EF ↑ ˜6% in STEMI over 6 mo (*JACC* 2007;50:149)

Medications (barring contraindications)

- **Aspirin:** 81 mg daily
- **$P2Y_{12}$ inhib** (ticagrelor or prasugrel preferred over clopi): treat for *at least* 12 mo Prolonged Rx beyond 12 mo → ↓ CV death, MI, & stroke (& stent thrombosis) w/ ↑ in bleeding, but no ↑ fatal bleeding or ICH. For Rx beyond 1st 12 mo, comparable efficacy w/ ticagrelor 90 or 60 mg bid, better safety & tolerability with 60 bid (*NEJM* 2015;372:1791; *JACC* 2007;49:1982 & 2015;65:2211).

  Some PPIs interfere w/ biotransformation of clopi and ∴ plt inhibition, but no convincing impact on clinical outcomes (*Lancet* 2009;374:989; *NEJM* 2010;363:1909); use w/PPIs if h/o GIB or multiple GIB risk factors (*JACC* 2010;56:2051)
- **β-blocker:** 23% ↓ mortality after MI
- **Statin:** high-intensity lipid-lowering (eg, atorvastatin 80 mg, *NEJM* 2004;350:1495)
- **Ezetimibe:** ↓ CV events including MI and ischemic stroke when added to statin (IMPROVE-IT, *NEJM* 2015;372:1500)
- **ACEI:** lifelong if HF, ↓ EF, HTN, DM; 4-6 wk or at least until hosp. d/c in all STEMI ? long-term benefit in CAD w/o HF (*NEJM* 2000;342:145 & 2004;351:2058; *Lancet* 2003;362:782)
- **Aldosterone antag:** 15% ↓ mortality if EF <40% & either s/s of HF or DM; contraindic if renal dysfxn (Cr >2.5 in men, >2 in women) or K >5 (*NEJM* 2003;348:1309)

- Nitrates: standing if symptomatic; SL NTG prn for all
- Ranolazine: inhibits late inward Na current, prevents intracellular Ca overload; ↓ recurrent ischemia (*JAMA* 2007;297:1775)
- Oral anticoagulants: if warfarin needed in addition to ASA/clopi (eg, AF or LV throm-bus), target INR 2-2.5. ? stop ASA if at high bleeding risk on triple Rx (*Lancet* 2013;381:1107). Not FDA approved: low-dose rivaroxaban (2.5 mg bid) in addition to ASA & clopi → 16% ↓ D/MI/stroke and 32% ↓ all-cause death, but ↑ major bleeding and ICH (*NEJM* 2012;366:9).
- NSAIDs/COX2 inhib relatively contraindic b/c ? ↑ death, MI, HF, rupture (*Circ* 2006;113:2906)

ICD (*NEJM* 2008;359:2245)

- If sust. VT/VF >2 d post-MI not due to reversible ischemia; consider wearable defibril-lator or ICD (*JACC* 2014;130:94)
- Indicated in 1° prevention of SCD if post-MI w/ EF ≤30-40% (NYHA II-III) or ≤30-35% (NYHA I); need to wait ≥40 d after MI (*NEJM* 2004;351:2481 & 2009;361:1427)

Risk factors and lifestyle modifications (*Circ* 2014;129(Suppl 2):S1 & S76)

- Low chol. (<200 mg/d) & fat (<7% saturated) diet; ? Ω-3 FA
- Traditional LDL-C goal <70 mg/dL; new recs w/o LDL-C target, rather simply high-intensity statin; may change w/ IMPROVE-IT trial showing that lower is better (lower CV event rate in arm with achieved LDL-C of 54 vs 70 mg/dL)
- BP <140/90 and consider <130/80 mmHg (HTN 2015;65:1372); smoking cessation
- If diabetic, tailor HbA1c goal based on Pt (avoid TZDs if HF)
- Exercise (30-60 min 5-7×/wk); cardiac rehab; BMI goal 18.5-24.9 kg/m^2
- Influenza & pneumococcal vaccination (*Circ* 2006;114:1549; *JAMA* 2013;310:1711); screen for depression

CARDIAC RISK ASSESSMENT FOR NONCARDIAC SURGERY

Goal: characterize risk of Pt & procedure → appropriate testing (ie, results will Δ management) and interventions (ie, reasonable probability of → risk of MACE)

Preoperative assessment

- Clinical assessment: evidence of active cardiac disease and/or risk factors
- Functional capacity (METs)
- Surgery-specific risk

Clinical Assessment

Active cardiac conditions	Clinical risk factors
• MI w/in 30 d or current unstable or severe angina	• h/o ischemic heart

- Decompensated HF
- Significant arrhythmia (eg, Mobitz II, high-grade AVB, 3° AVB, new or sx VT, SVT w/ HR >100, sx brady)
- Severe AS or sx MS

disease
- h/o congestive HF
- h/o stroke or TIA
- Diabetes on insulin
- Renal insuffic. (Cr >2 mg/dL)

Functional Capacity

1-4 METs (poor)	4-10 METs (moderate-to-good)	>10 METs (excellent)
• ADLs • Walk indoors • Walk 1-2 level blocks	• Climb a flight of stairs/hill • Walk briskly; heavy housework • Golf, doubles tennis	• Strenuous sports

Surgery-Specific Risk

High (>5% risk)	Intermediate (1-5%)	Low (<1%)
• Aortic or other major vascular • Peripheral vasc.	• Intrathoracic; intraperitoneal; prostate & major urologic • CEA; head & neck • Orthopedic	• Endoscopic • Breast; superficial • Cataract; ambulatory • Dental

Noninvasive Testing Result

High risk	Intermediate risk	Low risk
Ischemia at <4 METs *manifested* by ≥1 of: • Horiz/down ST ↓ ≥*1* mm or STE • ≥5 abnl leads or ischemic ECG Δs lasting >3 min after exertion • SBP ↓ 10 mmHg or typical angina	***Ischemia at* 4-6 *METs*** *manifested by ≥ 1 of:* • Horiz/down ST ↓ ≥1 mm • 3-4 abnl leads • 1-3 min after exertion	***No ischemia or at* >7 METs w/** • ST ↑ ≥1 mm or • 1-2 abnl leads

Imaging with excellent NPV, poor PPV. Consider if high-risk patient.

- **Revised Cardiac Risk Index** (RCRI): 6 risk factors = 5 clinical risk factors above and type of surgery

(intrathoracic, intra-abd, or suprainguinal vascular) (*Circ* 1999;100:1043) # of risk factors predicts risk of MACE: ≤1 RF → <1%, 2 RFs → 6.6%, ≥3 RFs → 11%

- Comorbidity indices (eg, Charlson index) may predict mortality (*Am J Med Qual* 2011;26:461)

Preoperative testing (*Circ* 2014;130:e278)

- ECG if known cardiac disease and possibly reasonable in all, except if low-risk surgery
- TTE if any of the following and prior TTE > 12 mo ago or prior to Δ in sx:

  dyspnea of unknown origin

  hx of HF w/ ↑ dyspnea

  suspected valvular disease (eg, murmur on exam)

  ≥moderate stenosis/regurg
- Stress test (usually pharmacologic) if:

  active cardiac issues where stress testing is indicated (qv), or not low-risk surgery, RCRI ≥2, poor or unknown fxnal capacity, and results *will Δ mgmt* (ie, modify or delay surgery, undergo coronary revascularization, etc.) overall low PPV to predict periop CV events
- Angiography: based on noninvasive stress results for standard indications, although systematic angio ↓ 2-5 y mortality in Pts undergoing vascular surgery (*JACC* 2009;54:989)
- ? consider CXR & ECG in preop evaluation of severely obese Pts (*Circ* 2009;120:86)

Coronary artery disease

- If possible, wait ˜60 d after MI in the absence of revascularization before elective surgery
- After PCI: delay elective surgery 14 d after balloon angioplasty, 30 d after BMS implantation, and ideally 6 mo after DES implantation

- Coronary revascularization should be based on standard indications (eg, ACS, refractory sx, lg territory at risk). Has not been shown to Δ risk of death or postop MI when done prior to elective vasc. surgery based on perceived cardiac risk (*NEJM* 2004;351:2795) or documented extensive ischemia (*AJC* 2009;103:897).

Heart failure

- Decompensated HF should be optimally treated prior to elective surgery
- ↓ EF (<30%) associated with poor outcomes
- 30-d CV event rate: symptomatic HF > asx HFrEF > asx HFpEF > no HF

Valvular heart disease

- If meet criteria for valve intervention (qv), do so before elective surgery (postpone if necessary)
- If severe valve disease and surgery urgent, intra- & postoperative hemodynamic monitoring reasonable (espec for AS, since at ↑ risk even if sx not severe; be careful to maintain preload, avoid hypotension, and watch for atrial fibrillation)
- If severe AS and Pt not eligible for or impractical to do AVR prior to noncardiac surgery, balloon aortic valvuloplasty (BAV) and transcatheter aortic valve replacement (TAVR) can be considered but not routinely

recommended (*Circ* 2008;118:e523)

Cardiac implantable electronic devices (CIEDs)

- Includes PPM, CRT, ICD
- Should be discussion between surgical team & CIED team regarding: need for device (eg, complete heart block) & consequences if interference w/ fxn likelihood of electromagnetic interference consideration of reprogramming, magnet use, etc.

Pre- & perioperative pharmacologic management

- **ASA:** continue in Pts w/ existing indication. Initiation just prior to surgery does not ↓ 30-d ischemic events and ↑ bleeding (*NEJM* 2014;370:1494), but Pts w/ recent stents excluded.
- **Dual antiplatelet therapy** in Pts undergoing urgent surgery: continue 4-6 wk after PCI (BMS or DES) unless risk of bleeding > benefit of prevention of stent thrombosis. If must discontinue ADP receptor blocker, continue ASA and restart ADP receptor blocker ASAP.
- **β-blockers** (*Circ* 2009;120:2123; *JAMA* 2010;303:551; *Am J Med* 2012;125:953) Continue βB in Pts on them chronically. Do not discontinue βB abruptly postop, as may cause sympathetic activation from withdrawal. Use IV agents peri-operatively if Pt unable to take PO.

  In terms of initiating βB, conflicting evidence; may depend on how administered. Some studies show ↓ death & MI (*NEJM* 1996;335:1713 & 1999;341:1789), another showed ↓ MI, but ↑ death & stroke and ↑ bradycardia/HoTN (*Lancet* 2008;371;1839).

  ? consider initiating if intermed- or high-risk ⊕ stress test, or RCRI ≥3, espec if vasc surgery

  Ideally initiate at least 1 wk prior to surgery, use low-dose, short-acting βB, and titrate slowly and carefully to achieve desired individual HR and BP goal (? HR ~55-65). Avoid bradycardia and HoTN.
- **Statins:** ↓ ischemia & CV events in Pts undergoing vascular surg (*NEJM* 2009;361:980); may reduce AF, MI, LOS in statin-naïve Pts (*Arch Surg* 2012;147:181). Consider in Pts w/ a clinical risk factor undergoing non-low-risk surgery.
- ACEI/ARB: may cause HoTN perioperatively. If held before surgery, restart ASAP.
- Amiodarone: ↓ incidence of postop AF

  oral (eg, 600 mg qd × 7 d preop, then 200 mg qd until discharge) & IV regimens equivalent but effective only if initiated ≥1 d prior to surgery (*Pacing Clin Electrophysiol* 2013;36:1017)

  cardiac surgery: ↓ postop AF, length of stay & cost (*NEJM* 1997;337:1785) thoracic surgery: ↓ postop AF but *not* length of stay or cost (*J Thorac* CV *Surg* 2010;140:45; *Ann Thorac Surg* 2012;94:339; *Eur J Cardiothorac Surg* 2014;45:120). Not advised if severe lung disease or undergoing pneumonectomy (*Ann Thorac Surg* 2011;92:1144).

Postoperative monitoring

- ✓ Postop ECG if known CAD or high-risk surgery. Consider if >1 risk factor for CAD.
- ✓ Postop troponin only if new ECG Δs or chest pain suggestive of ACS. Elevated Tn postop predicts mortality, but may simply be a marker for underlying CAD (*Annals* 2011;154:523; *JAMA* 2012;307:2295). Routine ✓ postop in all Pts (even just high-risk Pts) has not been proven to modify outcomes and it is not routinely recommended.

Myocardial, Valvular, and Pericardial Disease

HEART FAILURE

Definitions (*Braunwald's Heart Disease*, 10th ed., 2014)

- Failure of heart to pump blood forward at sufficient rate to meet metabolic demands of peripheral tissues, or ability to do so only at abnormally high cardiac filling pressures
- Low output (↓ cardiac output) vs high output (↑ stroke volume ± ↑ cardiac output)
- Left-sided (pulmonary edema) vs right-sided (↑ JVP, hepatomegaly, peripheral edema)
- Backward (↑ filling pressures, congestion) vs forward (impaired systemic perfusion)
- Systolic (inability to expel sufficient blood) vs diastolic (failure to relax and fill normally)
- Reduced (HFrEF) vs preserved (HFpEF) left ventricular ejection fraction
- Some degree of systolic and diastolic dysfxn may occur regardless of ejection fraction

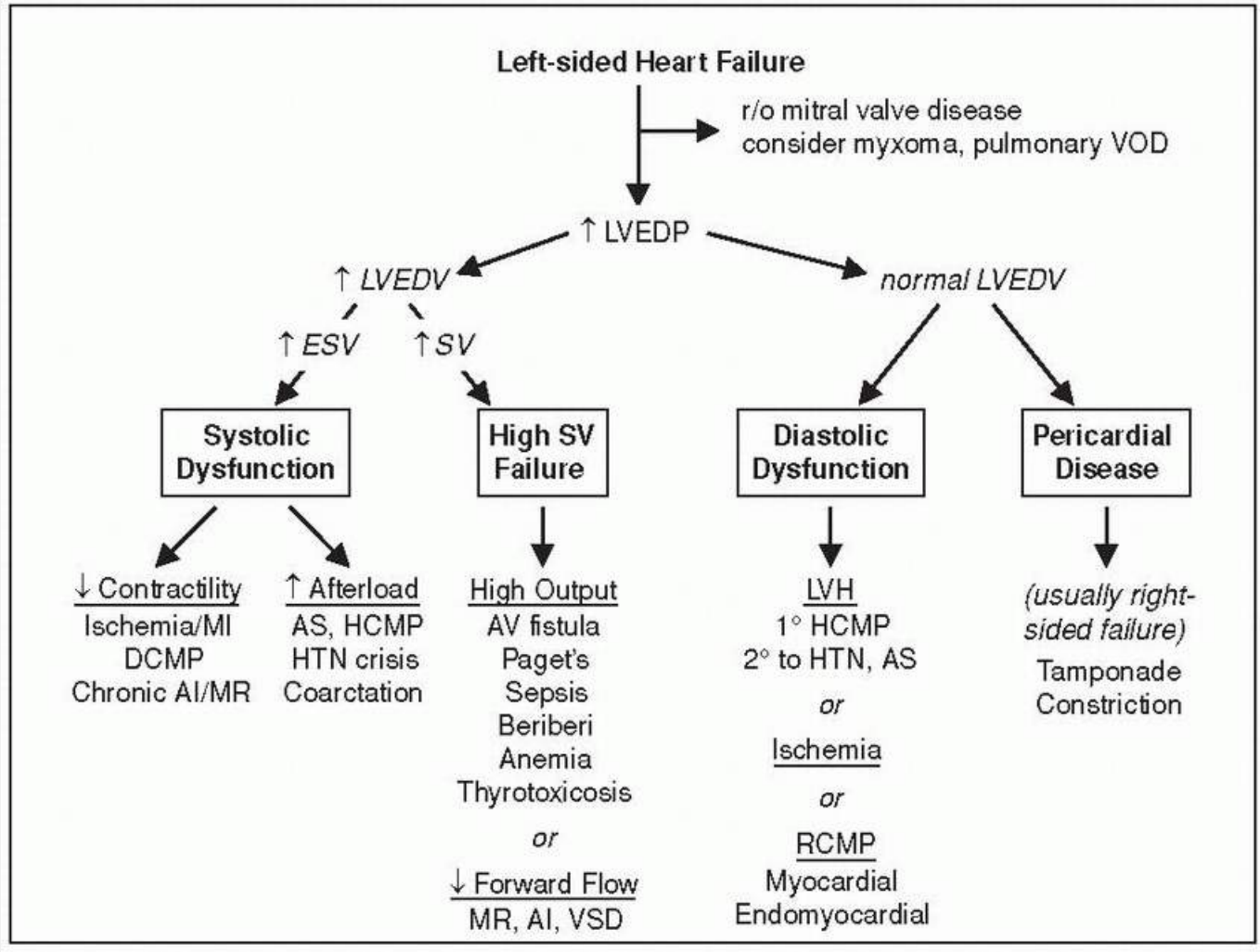


Figure 1-3 Approach to left-sided heart failure

History

- Low output: fatigue, weakness, exercise intolerance, Δ MS, anorexia
- Congestive: dyspnea, weight gain;

left-sided → orthopnea, paroxysmal nocturnal dyspnea

right-sided → peripheral edema, RUQ discomfort, bloating, early satiety

Stages in the Development of Heart Failure (*Circ* 2009;119:e391)

- A: At high **risk for HF**, but w/o structural heart disease or symptoms of HF
- B: **Structural heart disease**, but w/o signs or symptoms of HF
- C: Structural heart disease w/ prior or current **symptoms of HF**
- D: **Refractory heart failure** requiring specialized intervention

Functional classification (New York Heart Association class)

- Class I: no sx w/ ordinary activity; class II: sx w/ ordinary activity;

  class III: sx w/ minimal activity; class IV: sx at rest

Physical exam ("2-minute" hemodynamic profile; *JAMA* 1996;275:630 & 2002;287:628)

- **Congestion ("dry" vs "wet")**

  ↑ JVP (˜80% of the time RAP > 10 mmHg → PCWP >22 mmHg; *JHLT* 1999;18:1126)

  ⊕ hepatojugular reflux: ≥4 cm ↑ in JVP that persists for ≥15 sec w/ abdominal pressure Se/Sp 73/87% for RA >8 and Se/Sp 55/83% for PCWP >15 (*AJC* 1990;66:1002)

  Abnl Valsalva response: square wave (↑ SBP w/ strain), no overshoot (no ↑ BP after strain) S_3 (in Pts w/ HF → ˜40% ↑ risk of HF hosp. or pump failure death; *NEJM* 2001;345:574) rales, dullness at base 2° pleural effus. (*often absent* in chronic HF due to lymphatic compensation) ± hepatomegaly, ascites and jaundice, peripheral edema
- **Perfusion ("warm" *vs* "cold"): narrow pulse pressure (<25% of SBP) → CI <2.2 (91% Se, 83% Sp; *JAMA* 1989;261:884)**; other signs of low perfusion include soft S_1 (↑ dP/dt), pulsus alternans, cool & pale extremities, ↓ UOP, muscle atrophy
- Other signs to look for: periodic breathing/Cheyne-Stokes resp., abnl PMI (diffuse, sustained or lifting depending on cause of HF), S_4 (diast. dysfxn), murmur (valvular disease, ↑ MV or TV annulus, displaced papillary muscles), ↓ carotid upstroke

Evaluation for the presence of heart failure

- CXR (see Radiology insert): pulm edema, pleural effusions ± cardiomegaly, cephalization, Kerley B-lines
- BNP/NT-proBNP can help exclude HF; levels ↑ w/ age, renal dysfxn, AF, ↓ w/ obesity Se ≥95%, Sp ˜50%, PPV ˜65%, NPV ≥94% for HF in Pts p/w SOB (*BMJ* 2015;350:h910)
- Evidence of ↓ organ perfusion: ↑ Cr, ↓ Na, abnl LFTs
- Echo (see inserts): ↓ EF & ↑ chamber size ↑ systolic dysfxn; hypertrophy, abnl MV inflow, abnl tissue Doppler → ? diastolic dysfxn; abnl valves or pericardium; ↑ estimated RVSP
- PA catheterization: ↑ PCWP, ↓ CO and ↑ SVR (in low-output failure)

Evaluation of the potential causes of heart failure

- **ECG:** Q waves or PRWP (ischemic heart disease); LVH (hypertensive heart disease or HCM); low limb lead voltage (NICM or infiltrative); heart block (infiltrative)
- **TTE:** LV & RV size & function, valvular disease (and whether likely 1° or 2° to CMP), findings indicative of infiltrative or pericardial disease
- **Coronary angio** (or noninvasive imaging, eg, CT angio); if no CAD, w/u for NICM
- **Cardiac MRI:** multiparameter evaluation of cardiac structure & function including:

  LVEF, RVEF and volumes; regional wall motion abnormalities

  presence, pattern, & extent of myocardial scar (using late gadolinium enhancement, LGE) w/ Se/Sp of 100%/96% vs coronary angio for dx etiology of HF (*Circ* 2011;124:1351)

  myocardial inflammation or infiltration (eg, myocarditis, sarcoidosis, amyloidosis) restriction vs constrictive pericardial disease

Evaluation of Potential Causes of Heart Failure

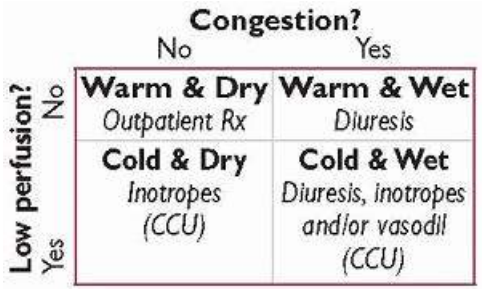
Etiology	ECG Pattern	Imaging Pattern
Ischemia, infarct	ST segment deviation, Qw	TTE: regional WMA, ± thinning/aneurysm Cor angio/CTA: obstructive CAD MRI: subendocardial or transmural LGE
Infiltrative	Low limb lead voltage, ± heart block, pseudoinfarct	TTE: LVH, "starry sky," ↑ biatrial size → amyloid MRI: inapprop nulling of myocardium + diffuse LGE → amyloid; patchy LV + RV LGE → sarcoidosis; ↓ T2 star → iron overload
Idiopathic DCM	Low limb lead volts, precordial LVH, BBB	TTE: 4 chamber dilation, diffuse hypokinesis MRI: mid-myocardial LGE
Tachy-myopathy	Persistent SVT	TTE: diffuse hypokinesis MRI: absent LGE in early stage
Myo(peri) -carditis	Pseudoischemia/-infarct. Pericard: diffuse concave STE w/ ST:T ratio >0.24 in V_6 and PR depression	TTE: typically global HK MRI: mid-myocardial + epicardial LGE, ↑ T2 and ↑ T1 ratios (edema)

Precipitants of acute heart failure

- **Dietary indiscretion or medical nonadherence** (˜40% of cases)
- **Myocardial ischemia or infarction** (˜10-15% of cases); myocarditis
- **Renal failure** (acute, progression of CKD, or insufficient dialysis) → ↑ preload

- **Hypertensive crisis (incl. from RAS), worsening AS** → ↑ left-sided afterload
- **Drugs** (βB, CCB, NSAIDs, TZDs), **chemo** (anthracyclines, trastuzumab), or **toxins** (EtOH)
- **Arrhythmias;** acute valv. dysfxn (eg, endocarditis), espec mitral or aortic regurgitation
- **COPD or PE** → ↑ right-sided afterload; **RV pacing**
- Other: **extreme emotional stress; anemia,** systemic **infection, thyroid** disease

Treatment of acute decompensated heart failure



- Assess degree of congestion & adequacy of perfusion
- For **congestion: "LMNOP"**

  Lasix IV w/ monitoring of UOP; total daily dose 2.5× usual daily PO dose → ↑ UOP, but transient ↑ in renal dysfxn vs 1× usual dose; Ø clear diff between cont gtt vs q12h dosing (*NEJM* 2011;364:797)

  Morphine (↓ sx, venodilator, ↓ afterload)

  Nitrates (venodilator)

  Oxygen ± noninvasive vent (↓ sx, ↑ P_aO_2; no Δ mortality; see "Mechanical Ventilation")

  Position (sitting up & legs dangling over side of bed → ↓ preload)

- For **low perfusion**, see below

- Adjustment of oral meds

  ACEI/ARB: hold if HoTN, consider Δ to hydralazine & nitrates if renal decompensation βB: reduce dose by at least ½ if mod HF, d/c if severe HF and/or need inotropes

Overview of Treatment of Heart Failure by Stage

Pt characteristics		Therapy
A	HTN, DM, CAD Cardiotoxin exposure FHx of CMP	Treat HTN, lipids, DM, SVT Stop smoking, EtOH; ↑ exercise ACEI/ARB if HTN/DM/CAD/PAD
B	Prior MI, ↓ EF, LVH or asx valvular dis.	All measures for stage A + ACEI/ARB & βB if MI/CAD or ↓ EF. ? ICD.
C	Overt HF	All measures for stage A, ACEI, βB, diuretics, Na restrict ↓ EF: aldo antag, ICD, consider CRT, nitrate/hydral, dig.

D	Sx despite max med Rx 4-y mortality >50%	All measures for stages A-C Consider IV inotropes, VAD, transplant, end-of-life care

- Utility of BNP-guided Rx remains debated (*Circ* 2013;301:500 & 509)
- Implantable PA pressure sensor in NYHA III → 37% ↓ risk of hosp (23% for HFrEF; 52% for HFpEF) (*Lancet* 2011;377:658)

Treatment of advanced heart failure (*Circ* 2009;119:e391)

- Consider PAC (qv) if not resp to Rx, unsure re: vol status, HoTN, ↑ Cr, need inotropes
- Tailored Rx w/ PAC; goals of MAP >60, CI >2.2 (MVO_2 >60%), SVR <800, PCWP <18
- **IV vasodilators:** NTG, nitroprusside (risk of coronary steal if CAD; prolonged use → cyanide/thiocyanate toxicity); nesiritide (rBNP) not rec for routine use (*NEJM* 2011;365:32)
- **Inotropes:** in addition to ↑ inotropy, consider additional properties:

  dobutamine: vasodilation at doses ≤5 mcg/kg/min; mild ↑ PVR; desensitization over time

  dopamine: splanchnic vasodil. → ↑ GFR & natriuresis; vasoconstrictor at ≥5 mcg/kg/min; does not enhance decongestion or preserve renal fxn in ADHF (*JAMA* 2013;310:2533)

  milrinone: prominent systemic & pulmonary vasodilation; ↑ dose by 50% in renal failure
- Ultrafiltration: similar wt loss to aggressive diuresis, but ↑ renal failure (*NEJM* 2012:367:2296)
- **Mechanical circulatory support (MCS)** (*JHLT* 2013;32:157; *JACC* 2015;65:e7 & 2542)

  Temporary MCS*:* depending on the device (Table), can be placed percutaneously or surgically to support LV or RV, as a bridge to recovery, for periprocedural support, or as a bridge to decision regarding transplant or durable long-term MCS

  Intra-aortic balloon pump (IABP): inflates in diastole & deflates in systole to ↓ impedance to LV ejection of blood, ↓ myocardial O_2 demand & ↑ coronary perfusion

  Axial flow pumps (eg, Impella): Archimedes screw principle in LV

  Extracorporeal magnetically levitated centrifugal pumps (eg, TandemHeart & CentraMag)

  Extracorporeal membrane oxygenation (ECMO, *Circ* 2015;131:676)

Short-Term Mechanical Circulatory Support in Cardiogenic Shock

Device	IABP	Impella 2.5 & CP	Impella 5.0	Tandem	CentriMag	ECMO
Max support (L/min)	0.5	2.5 & 3-4	5.0	5.0	10	6
RV support	N	Y (2^{nd} dev.)	N	Y (2^{nd} dev.)	Y (2^{nd} dev.)	Y

Support duration	wks	~4 wk	~4 wk	<4 wk	mos	wks
Percutan?	Y	Y	N	Y	N	Y
Contraindic.	≥ mod AI, severe PAD	LV thrombus, mech AV, severe AS		coagulop severe PAD	coagulop	coagulop

(*Circ* 2011;123:533 & 126:1717; *JACC* 2015;65:e7)

Durable Long-term MCS*:* surgically placed LVAD ± RVAD as bridge to recovery (*NEJM* 2006;355:1873) or transplant (HeartMate II or HeartWare LVAD or Total Artificial Heart if biventricular failure), or as destination Rx (HeartMate I: 52% ↓ 1-y mort. vs med Rx; *NEJM* 2001;345:1435, HeartMate II: 24% ↑ mort. vs HeartMate 1; *NEJM* 2009;361:2241)

- **Cardiac transplantation:** curative Rx but supply of organs limited (~2500/y in U.S.) 10% mortality in 1st year, median survival ~10 y

  Contraindications: active malignancy or infection, irreversible PHT (TPG>15, PVR>5WU despite pulmonary vasodilator Rx), active substance abuse or lack of social supports

  Relative contraindications: age (eg, >70 y), other end organ dysfunction (liver, kidney, lung, unless dual organ transplantation is performed)

Treatment of Chronic Heart Failure with Reduced Ejection Fraction

Diet, exercise	Na <2 g/d, fluid restriction, exercise training in ambulatory Pts
ACEI	↓ mortality: 40% in NYHA IV, 16% in NYHA II/III, 20-30% in asx but ↓ EF (*NEJM* 1992;327:685 & *Lancet* 2000;355:1575) High-dose more effic. than low. Watch for ↑ Cr, ↑ K (ameliorate by low-K diet, diuretics, Kayexalate; patiromer, another K binder, under review; *NEJM* 2015;372:211), cough, angioedema.
ATII receptor blockers (ARBs)	*Consider as alternative if cannot tolerate ACEI (eg, b/c cough)* Noninferior to ACEI (*Lancet* 2000;355:1582 & 2003;362:772) As with ACEI, higher doses more efficacious (*Lancet* 2009;374:1840) Adding to ACEI → ↑ risk of ↑ K and ↑ Cr (*BMJ* 2013;346:f360)
ARNi (ARB + neprilysin inhib)	Neutral endopeptidase (NEP, aka neprilysin) degrades natriuretic peptides as well as bradykinin & angiotensins. LCZ696 = valsartan + sacubitril (NEPi): ↓ CV mort & HF hosp c/w ACEi; more HoTN and trend to more angioedema (PARADIGM-HF, *NEJM* 2014;371:993).
Hydralazine + nitrates	*Consider if cannot tolerate ACEI/ARB or in blacks w/ NYHA III/IV* 25% ↓ mort. (*NEJM* 1986;314:1547); infer. to ACEI (*NEJM* 1991;325:303) 43% ↓ mort. in blacks on standard Rx (A-HEFT, *NEJM* 2004;351:2049)

β-blocker (data for carvedilol, metoprolol, bisoprolol)	*EF will transiently* ↓, *then* ↑. *Contraindic. in decompensated HF.* 35% ↓ mort. & 40% ↓ rehosp. in NYHA II-IV (*JAMA* 2002;287:883) Carvedilol superior to low-dose metop in 1 trial (*Lancet* 2003;362:7), but meta-analysis suggests no diff between βB (*BMJ* 2013;346:f55).
Aldosterone antagonists	*Consider if adeq. renal fxn and w/o hyperkalemia; watch for* → *K* 24-30% ↓ mort. in NYHA II-IV & EF ≤35% (*NEJM* 2011;364:11) 15% ↓ mort. in HF post-MI, EF ≤40% (EPHESUS, *NEJM* 2003;348:1309)
Cardiac resynch therapy (CRT, qv)	*Consider if EF* ≤35%, *LBBB and symptomatic HF* 36% ↓ mort. & ↑ EF in NYHA III-IV (CARE-HF, *NEJM* 2005;352:1539) 41% ↓ mort. if EF ≤30%, LBBB and NYHA I/II (*NEJM* 2014;370:1694)
ICD (see "Cardiac Rhythm Mgmt Devices")	*Use for* 1° *prevention if EF* ≤30-*35% or 2° prevention; not if NYHA IV* ↓ mort. in ischemic & non-isch CMP; no Δ mort. early post-MI (*NEJM* 2004;351:2481 & 2009;361:1427), ∴ wait ≥40 d
Diuretics	Loop ± thiazide diuretics (sx relief; no mortality benefit)
Digoxin	23% ↓ HF hosp., no Δ mort (*NEJM* 1997;336:525); ? ↑ mort w/ ↑ levels (*NEJM* 2002;347:1403); optimal 0.5-0.8 ng/mL (*JAMA* 2003;289:871)
Ivabradine (*If* blocker w/o ⊖ ino)	*Consider if HR* >70, *NSR on max βB.* 18% ↓ CV mort or HF hosp (*Lancet* 2010;376:875)
ω-3 fatty acids	9% ↓ mortality (included HF with normal LVEF) (*Lancet* 2008:372:1223)
IV iron supplementation	*? if NYHA II/III, EF* ≤40%, *Fe-defic* (ferritin <100 or ferritin 100-300 & TSAT <20%). ↓ Sx, ↑ 6MWD, independent of Hct (*NEJM* 2009;361:2436).
Anticoagulation	*If AF, VTE, LV thrombus,* ± *if large akinetic LV segments* In SR w/ EF <35%, ↓ isch stroke, but ↑ bleed (*NEJM* 2012;366:1859)
Heart rhythm	Catheter ablation of AF → ↑ in EF, ↓ sx (*NEJM* 2004;351:2373) No mortality benefit to AF rhythm vs rate cntl (*NEJM* 2008;358:2667) Pulm vein isolation ↓ sx c/w AVN ablation & CRT (*NEJM* 2008;359:1778)
Meds to avoid	NSAIDs, nondihydropyridine CCB, TZDs
Experimental	Serelaxin ± ↓ dyspnea & ? ↓ mortality (*Lancet* 2013;381:29)

(*Circ* 2009;119:e391; *NEJM* 2010;362:228; *Lancet* 2011;378:713 & 722)

Heart failure with preserved EF (HFpEF; "Diastolic HF") (*Circ* 2011;124:e540)

- Epidemiology: ~½ of Pts w/ HF have normal or only min. impaired systolic fxn (EF ≥40%); risk factors for HFpEF incl ↑ age, ♀, DM, AF. Mortality ≈ to those w/ systolic dysfxn.
- Etiologies (impaired relaxation and/or ↑ passive stiffness): ischemia, prior MI, LVH, HCMP infiltrative CMP, RCMP aging, hypothyroidism
- Precipitants of pulmonary edema: *volume overload* (poor compliance of LV → sensitive to even modest ↑ in volume); *ischemia* (↓ relaxation); *tachycardia* (↓ filling time in diastole), AF (loss of atrial boost to LV filling); HTN (↓ afterload → ↓ stroke volume)
- Dx w/ clinical s/s of HF w/ preserved systolic fxn. Dx supported by evidence of diast dysfxn:

  (1) echo: abnl MV inflow (E/A reversal and Δs in E wave deceleration time) & ↓ myocardial relax. (↑ isovol relax. time & ↓ early diastole tissue Doppler velocities)

  (2) exercise-induced ↑ PCWP (± ↓ response chronotropic & vasodilator reserve)
- Treatment: diuresis for vol overload, BP control, prevention of tachycardia and ischemia; no benefit to: ACEI/ARB (*NEJM* 2008;359:2456) or PDE5 inhib (*JAMA* 2013;309:1268) spironolactone ↓ CV death & HF hosp (at least in Americas) (*NEJM* 2014;370:1383);

  ARNi (*Lancet* 2012;380:1387) and serelaxin (*Lancet* 2013;381:29) under study

PA CATHETER AND TAILORED THERAPY

Rationale

- Cardiac output (CO) = SV × HR; LV SV depends on LV end-diastolic volume (LVEDV) ∴ manipulate LVEDV to optimize CO while minimizing pulmonary edema
- Balloon at tip of catheter inflated → floats into "wedge" position. Column of blood extends from tip of catheter, through pulmonary circulation, to a point just proximal to LA. Under conditions of no flow, PCWP ≈ LA pressure ≈ LVEDP, which is proportional to LVEDV.
- Situations in which these basic assumptions fail:

  (1) Catheter tip not in West lung zone 3 (and ∴ PCWP = alveolar pressure ≠ LA pressure); clues include lack of *a* & *v* waves and if PA diastolic pressure < PCWP

  (2) PCWP > LA pressure (eg, mediastinal fibrosis, pulmonary VOD, PV stenosis)

  (3) Mean LA pressure > LVEDP (eg, MR, MS)

  (4) Δ LVEDP-LVEDV relationship (ie, abnl compliance, ["nl" LVEDP may not be optimal)

Indications (*Circ* 2009;119:e391; *NEJM* 2013;369:e35)

- **Diagnosis and evaluation**

  Ddx of shock (cardiogenic vs distributive; espec if trial of IVF failed or is high risk) and of pulmonary edema (cardiogenic vs not; espec if trial of diuretic failed or is high risk)

  Evaluation of CO, intracardiac shunt, pulmonary HTN, MR, tamponade, cardiorenal syndrome

  Evaluation of unexplained dyspnea (PAC during provocation w/ exercise, vasodilator)
- **Therapeutics** (*Circ* 2006;113:1020)

Tailored therapy to optimize PCWP, SV, $S_{MV}O_2$, RAP, & PVR, in heart failure or shock

Guide to vasodilator therapy (eg, inhaled NO) in pulm HTN, RV infarction

Guide to perioperative management in some high-risk Pts, pretransplantation

Guide to candidacy for thoracic organ transplantation and mechanical circulatory support

- **Contraindications**

  Absolute: right-sided endocarditis, thrombus/mass or mechanical valve; PE

  Relative: coagulopathy (reverse), recent PPM or ICD (place under fluoroscopy), LBBB (˜5% risk of RBBB ↑ CHB, place under fluoro), bioprosthetic R-sided valve

Efficacy concerns (*NEJM* 2006;354:2213; *JAMA* 2005;294:1664)

- No benefit to routine PAC use in high-risk surgery, sepsis, ARDS
- No benefit in decompensated HF (*JAMA* 2005;294:1625); untested in cardiogenic shock
- But: ˜½ of CO & PCWP clinical estimates incorrect; CVP & PCWP not well correl.; ∴ use PAC to (a) answer hemodynamic ? and then remove, or (b) manage cardiogenic shock

Pulmonary Artery Catheter Features

Component	cm from distal tip	Function
Distal lumen	0	Sampling of blood for $S_{MV}O_2$
1.5-mL balloon	0.5	Inflation allows flow directed placement & determination of PCWP
Thermistor	4	Detection of temp Δ for CO calc
Proximal injectate port	26	Infusions & injection of saline for CO calc
Additional Optional Features		
Fiberoptic O_2 sat sensor	0	Allows continuous measurement of $S_{MV}O_2$
Thermal filament	˜10-25	Allows continuous CO calc by thermodilution
Pacing port	˜19	Allows placement of pacing wire in RV
Infusion port(s)	˜30	Additional infusion port(s)

Placement

- Insertion site: **R internal jugular** or **L subclavian veins** for "anatomic" flotation into PA
- **Inflate** balloon (max 1.5 mL) when **advancing** and to **measure PCWP**
- Use resistance to inflation and pressure tracing to avoid overinflation & risk of PA rupture
- Should require 1-1.5 mL air in balloon to float into wedge (<1 mL → pull PAC back; no PCWP at 1.5 mL → advance)
- **Deflate** balloon when **withdrawing** and at all other times
- CXR should be obtained after placement to assess for catheter position and PTX
- If catheter cannot be successfully floated (typically if severe TR or RV dilatation) or if another relative contraindication exists, use fluoroscopic guidance

Complications

- **Central venous access:** pneumo/hemothorax (~1%), arterial puncture (if inadvertent cannulation w/ dilation → surgical/endovasc eval), air embolism, thoracic duct injury
- **Arrhythmias:** ½ PVCs, 20% NSVT, 3% VT (minimize time PAC tip in RV); RBBB (5%)

- **Inability to advance:** difficulty RA → RV seen w/ lg RA and/or severe TR; difficulty RV → PA seen w/ lg RV; deflate balloon, withdraw 10 cm, inflate balloon & readvance. *If repeated attempts unsuccessful at bedside, then perform under fluoro* (to avoid PAC coiling & potentially knotting, which would require interventional cardiology to extract).
- **PA rupture:** risk factors include prolonged balloon inflation, PHT, anticoag. Presents w/ hemoptysis and, if severe, hypoxemia & hypovolemic shock. *Keep balloon inflated, intubate w/ dbl-lumen endotracheal tube, lateral decubitus position with affected side down, STAT interventional radiology and/or thoracic surgery consultation.*
- **Air embolism:** presents w/ dyspnea, chest pain, ↑ R-sided pressures, HoTN. *Place in Trendelenburg, high-flow* O_2.
- **Other:** infxn (espec if PAC >3 d old); thrombus; pulm infarction; valve/chordae damage

Intracardiac pressures

- Zero the transducer and level it with the right atrium (phlebostatic axis)
- Transmural pressure (≈ preload) = measured intracardiac pressure - intrathoracic pressure
- Intrathoracic pressure (usually slightly ⊖) is transmitted to vessels and heart
- **Always measure intracardiac pressure at end-expiration**, when intrathoracic pressure closest to 0 ("high point" in spont. breathing Pts; "low point" in Pts on ⊕ pressure vent.)
- If ↑ intrathoracic pressure (eg, PEEP), measured PCWP *overestimates* true transmural pressures. Can approx by subtracting ~½ PEEP (× ¾ to convert cm H2O to mmHg).
- PCWP: LV preload best estimated at *a* wave; risk of pulmonary edema from avg PCWP

Cardiac output

- **Thermodilution:** saline injected in RA. Δ in temp over time measured at thermistor (in PA) is integrated and is ≈ 1/CO. Inaccurate if ↓ CO, severe TR or shunt.
- **Fick method:** O_2 consumpt ([V with dot above]O_2) (L/min) = CO (L/min) × Δ arteriovenous O_2 content

  ∴ CO = [V with dot above]O_2 /C(a-v)O_2

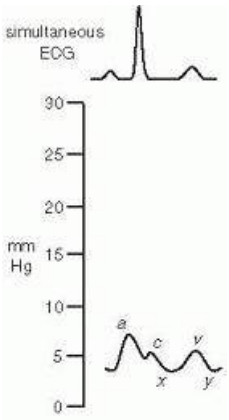
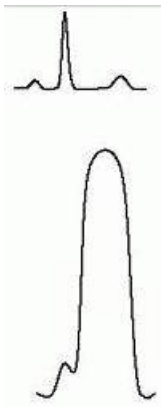
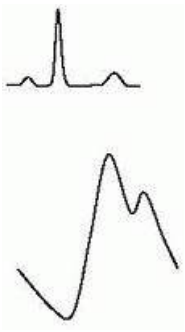
  [V with dot above]O_2 ideally measured (espec if ↑ metab demands), but freq estimated (125 mL/min/m^2)

  C(a-v)O_2 = [10 × 1.36 mL O_2/g of Hb × Hb g/dL × (S_aO_2-$S_{MV}O_2$)]

  $S_{MV}O_2$ is key variable that Δs *with acute interventions*

  If $S_{MV}O_2$ >80%, consider if the PAC is "wedged" (ie, pulm vein sat), L→ R shunt, impaired O_2 utilization (severe sepsis, cyanide, carbon monoxide), ↑ ↑ FiO_2

PA Catheter Waveforms

Location	RA	RV	PA	PCWP
Distance	~20 cm	~30 cm	~40 cm	~50 cm
Normal Pressure (mmHg)	mean ≤6	syst 15-30 diast 1-8	syst 15-30 mean 9-18 diast 6-12	mean ≤12
Waves				
Comment	*a* = atrial contraction, occurs in PR interval *c* = bulging of TV back into RA at start of systole *x* = atrial relaxation and descent of base of heart *v* = blood entering RA, occurs mid-T wave *y* = blood exiting RA after TV opens at start of diastole	RVEDP occurs right before upstroke and ≥ mean RA pressure unless there is TS or TR	Waveform should contain notch (closure of pulmonic valve). Peak *during* T wave PA systolic = RV systolic unless there is a gradient (eg, PS). PA diastolic ≈ PCWP unless ↑ trans-pulm gradient (eg, ↑ PVR).	Similar to RA except *dampened* and *delayed. a* wave *after* QRS, ± distinct *c* wave, *v* wave *after* T (helps distinguish PCWP w/ large *v* waves 2° MR from PA).

PCWP waveform abnormalities: large *a* wave → ? mitral stenosis; large *v* wave → ? mitral regurgitation; blunted *y* descent → ? tamponade; steep *x* & *y* descents → ? constriction.

Hemodynamic Profiles of Various Forms of Shock

Type of shock	RA	PCWP	CO	SVR
Hypovolemic	↓	↓	↓	↓
Distributive	variable	variable	usually ↑ (but can be ↓ in sepsis)	↓
Cardiogenic: 1° L-sided (eg, acute MI)	nl or ↑	↑	↓	↑
Cardiogenic: 1° R-sided (eg, RV infarct; PE)	↑	nl or ↓	↓	↑
Tamponade	↑	↑	↓	↑

Surrogates: JVP ≈ RA; pulmonary edema on CXR implies ↑ PCWP; UOP ∝ CO (barring AKI); delayed capillary refill (ie, >2-3 sec) implies ↑ SVR

Tailored therapy and management of shock (*Circ* 2009;119:e391)

- **Goals:** optimize both MAP and CO to promote end-organ perfusion, while ↓ risk of pulmonary edema & systemic venous congestion MAP = CO × SVR; CO = HR × SV (depends on preload, afterload and contractility) pulmonary edema when PCWP >20-25 (↑ levels may be tolerated in chronic HF) hepatic and renal congestion when CVP/RAP >15 mmHg
- **Optimize preload** = LVEDV ≈ LVEDP ≈ LAP ≈ PCWP (*NEJM* 1973;289:1263) goal **PCWP ˜14-18 in acute MI,** ≤1 **4 in acute decompensated HF** optimize in individual Pt by measuring SV w/ different PCWP to create Starling curve ↑ by giving NS (albumin w/o clinical benefit over NS; PRBC if significant anemia) ↓ by diuresis (qv), ultrafiltration or dialysis if refractory to diuretics
- **Optimize afterload** ≈ wall stress during LV ejection = [(˜SBP × radius) / (2 × wall thick.)] and ∴ ∝ MAP and ∝ SVR = (MAP - CVP / CO); goals: **MAP >60, SVR 800-1200** MAP >60 & SVR ↑ : vasodilators (eg, nitroprusside, NTG, ACEI, hydral.) or wean pressors MAP <60 & SVR ↑ (& ∴ CO ↓): temporize w/ pressors until can ↑ CO (see below) MAP <60 & SVR low/nl (& ∴ inappropriate vasoplegia): vasopressors (eg, norepinephrine [α, β], dopamine [D, α, β], phenylephrine [α] or vasopressin [V_1] if refractory)
- **Optimize contractility** ∝ CO for given preload & afterload; **goal CI = (CO / BSA) >2.2** if too low despite optimal preload & vasodilators (as MAP permits):

  ⊕ *inotropes:* eg, dobutamine (mod inotrope & mild vasodilator) or milrinone (strong inotrope & vasodilator, incl

pulm), both proarrhythmic, or epi (strong inotrope & pressor)

mechanical support devices: eg, IABP, percutaneous or surgical VAD (L-sided, R-sided, or both) or ECMO (*Circ* 2011;123:533)

Vasopressors and Inotropes Used in Shock

Drug	Receptors			Hemodynamics				Comment
	α_1	β_1	β_2	SVR	MAP	HR	CO	
Phenylephrine	+++	0	0	↑↑↑	↑↑	↓↓[a]	↓[a]	↑ PVR
Vasopressin[b]	0	0	0	↑↑↑	↑↑	↓↓[a]	↓[a]	↔PVR; ∴ attractive if RV dysfxn or PHT
Norepinephrine	+++	++	+	↑↑↑	↑↑	↔/↑	↔/↑	Better outcomes than w/ dopa
Epinephrine	+++	+++	+++	↓ / ↑[c]	↑	↑↑	↑	β predom at low doses
Isoproterenol	0	+++	+++	↓↓	↓	↑↑ ↑	↑↑	⊕ chronotrope
Dobutamine	+	+++	++	↓	↔/↓	↑↑	↑↑	↓ PCWP
Dopamine[d]	+	++	0	↔/↑[d]	↔/↑[d]	↑↑ ↑	↑	
Milrinone[e]	0	0	0	↓↓	↓	↔	↑↑ ↑	↓↓ PCWP; ↓ PVR; ∴ attractive if RV dysfxn or PHT

[a]Bradycardia seen due to vagal reflex if hypertension; ↓ CO due to ↑ afterload

[b]V_1 agonist

[c]Low doses ↓ SVR, high doses ↑ SVR

[d]Also a (D) dopa receptor agonist; 0.5-2 mcg/kg/min → D; 2-10 → D & β_1; > 10 → α_1, β_1, D

[e]PDE_3 inhibitor

CARDIOMYOPATHIES

Diseases with mechanical and/or electrical dysfunction of the myocardium

DILATED CARDIOMYOPATHY (DCM)

Definition and epidemiology (*Circ* 2013;128:e240; *JACC* 2013;62:2046)

- Ventricular dilatation and ↓ contractility ± ↓ wall thickness *in the absence of myocardial disease caused by ischemia/infarct, valvular disease or hypertension*
- Ventricular dysfunction usually global but can be regional variation
- May be accompanied by significant MR & TR due to impaired leaflet coaptation
- Incidence: 5-8/100,000/y; prevalence: 1/2500. Most common reason for heart transplant.

Etiologies (*JACC* 2011;57:1641; *Circ Res* 2012;111:131)

- **Familial** (>35%): defined as having DCM and at least 2 closely related family members with otherwise unexplained DCM; usually autosomal dominant pattern of inheritance; ~30 genes identified to date, encoding structural & nuclear proteins *sarcomere:* eg, titin (*TTN,* ~20%; *NEJM* 2012;366:619); β- & α-myosin heavy chain (*MYH7, MYH6,* ~5% each); troponin T (*TNNT2,* ~5%)

  nuclear envelope: eg, lamin A/C (*LMNA,* ~5%), often w/ conduction system disease (eg, sinus brady, AV block, atrial arrhythmias) (*NEJM* 2009;341:1715)

  ion channel: eg, Na channel (*SCN5A,* <5%), same gene as for LQTS & Brugada *Z-disc:* eg, myopalladin (*MYPN,* <5%), ankyrin (*ANKRD1,* <5%) *cytoskeletal:* eg, desmin (DES, <1%); dystrophin (*DMD,* <1%) *syndromic disorders:* eg, muscular dystrophies (Duchenne/Becker; limb-girdle)
- **Idiopathic** (<20%): ? undiagnosed infectious, alcoholic or genetic cause (in ~1/4 of Pts w/ "idiopathic" DCM, evidence of DCM found in 1° relative, suggesting undx genetic)
- **Infectious myocarditis** (10-15%, autoimmune response; *Lancet* 2012;379:738)

  Viruses (parvoB19 & HHV6 > coxsackie, adeno, echo, CMV, HCV): from subacute (dilated LV; mild-mod dysfxn) to fulminant (nondil., thick, edematous LV; sev dysfxn)

  Bacterial, fungal, rickettsial, TB, Lyme (mild myocarditis, often with AVB, qv)

  HIV: ~8% of asx HIV ⊕; due to HIV, 2° infxns, or antiretrovirals; HIV also associated w/ premature CAD (*JACC* 2012;59:779)

  Chagas: apical aneurysm ± thrombus, RBBB, megaesophagus/colon (*NEJM* 2015;373:456)
- **Toxic**

  alcohol (20-35%; *Prog* CV *Dis* 2010;52:289): typically 7-8 drinks/d × >5 y, but variable; male > female, typical age 30-55, may resolve w/ abstinence

  cocaine (primarily myocardial ischemia, but DCM is also seen); amphetamines & ephedra; anabolic steroids

  XRT (usually RCM); cobalt; chloroquine anthracyclines: risk ↑ >550 mg/m^2, may manifest late; usually irreversible cyclophosphamide, taxoids, mitomycin-C, 5-fluorouracil, and interferons trastuzumab: usually reversible
- **Infiltrative** (5%): often mix of DCM + RCM (qv) with thickened walls sarcoidosis, amyloidosis, hemochromatosis, tumor

- **Autoimmune**

  collagen vasc. dis./vasculitis (˜5%): PM, SLE, scleroderma, PAN, RA, Wegener's;

  peripartum (last month → 5 mo postpartum; *EHJ* 2015;36:1090): ˜1:3000 preg. ↑ risk w/ multiparity, ↑ age, Afr Am; stnd HF Rx except if preg then select drugs based on safety; ? bromocriptine to ↓ prolactin; 72% normalize EF; predictors of poor recovery include EF <30% & LVEDD ≥6 cm (*JACC* 2015;66:905); even if nl EF, ˜30% recur w/ next preg

  idiopathic giant cell myocarditis (GCM): avg age 42 y, may present as severe HF, high-grade AV block, or VT, historically poor prognosis (<6 mo median transplant-free survival; *NEJM* 1997;336:1860), but with modern immunosuppression 67% achieve HF remission with transplant-free survival of 77% at 1 y (*Circ* HF 2013;6:15)

  eosinophilic (variable peripheral eos): hypersensitivity (mild HF but at risk for SCD) or acute necrotizing eosinophilic myocarditis (ANEM; STE, effusion, severe HF)

- **Stress-induced** (Takotsubo = apical ballooning)

  typically seen in postmenopausal ♀ after psychological stressor

  ? due to catecholamine surge → microvasc dysfxn & Ca overload mimics MI (pain, ± STE & ↑ Tn; deep TWI & ↑ QT); mid/apex dyskinesis, sometimes w/ cardiogenic shock (caution w/ pressors as can induce LV outflow tract obstruction)

  ? Rx w/ βB, ACEI, anticoag if LV thrombus (but usually not just for dyskinesis given rapid resolution); usually improves over wks (*JAMA* 2011;306:277)

- **Tachycardia:** likelihood ∝ duration & rate (although avg HR ˜120); often resolves w/ rate control, which is only way to definitely make dx, over several mos (*Circ* 2005;112:1092)

- **Arrhythmogenic (right ventricular) cardiomyopathy** (ACM, formerly ARVC): see below

- **Metabolic/other**

  hypothyroidism, acromegaly, pheo; OSA; cirrhosis thiamine, selenium or carnitine deficiency

- **LV noncompaction:** see below

Clinical manifestations

- **Heart failure:** both congestive & poor forward flow sx; signs of L- & R-sided HF **diffuse**, **laterally displaced PMI**, **S3**, ± MR or TR (annular dilat., displaced pap. muscle)
- Embolic events (˜10%), supraventricular/ventricular arrhythmias, & palpitations
- Chest pain can be seen w/ some etiologies (eg, myocarditis)

Diagnostic studies and workup

- CXR: moderate to marked cardiomegaly, ± pulmonary edema & pleural effusions
- ECG: may see PRWP, Q waves or BBB; low-voltage; AF (20%); may be normal
- Echocardiogram: LV dilatation, ↓ EF, *regional or global* LV HK ± RV HK, ± mural thrombi
- Cardiac MRI: up to 76% Se, 96% Sp for myocarditis or infiltrative disease (*JACC Imaging* 2014;7:254); nontransmural delayed gadolinium enhancement in *noncoronary* distribution suggestive of DCM; extent of midwall fibrosis correlated w/ mortality in NICM (*JAMA* 2013;309:896)

- Laboratory evaluation: TFTs, iron studies, HIV, SPEP, ANA; others per clinical suspicion; viral serologies *not* recommended (*JACC* 2012;59:779)
- Stress test: useful to r/o ischemia (low false ⊖ rate), high false ⊕ rate, even w/ imaging
- Coronary angiography to r/o CAD if risk factors, h/o angina, Qw MI on ECG, equivocal ETT; consider CT angiography (*JACC* 2007;49:2044)
- ? Endomyocardial biopsy (*JACC* 2007;50:1914)

  yield 10%: of these, 75% myocarditis (for which no proven Rx) & 25% systemic disease

  40% false ⊖ rate (patchy dis.) & false ⊕ (necrosis → inflammation)

  ∴ biopsy if: acute & hemodynamic or electrical compromise (r/o GCM, ANEM); arrhythmia or RCMP features (r/o infiltrative); or suspect toxic, allergic, tumor
- Family hx & genetic testing (*JAMA* 2009;302:2471; *Circ* 2013;128:e240)

  family hx for ≥3 generations; incomplete penetrance and variable expression make dx of familial CMP challenging

  sequencing of DCM gene panels now available; typically test most clearly affected person

  if specific mutation identified, then can screen family using genetic testing

  if no mutation identified, consider cascade clinical screening (ECG, echo) of 1° relatives every ~3-5 years

Treatment (see "Heart Failure" for standard HF Rx)

- Implantation of devices may be tempered by possibility of reversibility of CMP
- Immunosuppression: for giant cell myocarditis (prednisone + AZA + cyclosporine), collagen vasc disease, peripartum (? IVIg), & eosinophilic; no proven benefit for viral myocarditis
- Prognosis differs by etiology (*NEJM* 2000;342:1077): postpartum (best), ischemic/GCM (worst)
- Abstain from EtOH (for alcoholic CMP and reasonable for others)
- Consider ACEI and/or βB if genotype ⊕ but currently phenotype ⊖

HYPERTROPHIC CARDIOMYOPATHY (HCM)

Definition and epidemiology

- LV (usually ≥15 mm) and/or RV hypertrophy disproportionate to hemodynamic load
- Prevalence: 1/500; 50% sporadic, 50% familial, most asymptomatic
- Autosomal-dominant mutations (> 1500) in cardiac sarcomere genes most common genes involved: β-myosin heavy chain (*MYH7,* ~40%), myosin-binding protein C (*MYBPC3,* ~40%), cardiac troponin T (*TNNT2,* ~5%) and I (*TNNI3,* ~5%) no clear correlation between genotype and clinical course
- Noonan syndrome: HCM, pulmonic stenosis, ASD, short stature, pectus, webbed neck
- Ddx: LVH 2° to HTN, AS, elite athletes (wall usually <13 mm & symmetric and nl/↑ rates of tissue Doppler diastolic relaxation; LV cavity large; no late gadolinium enhancement on MRI; *Circ* 2011;123:2723), Fabry dis. (↑ Cr, skin findings)

Pathology

- Myocardial fiber disarray with hypertrophy, which creates arrhythmogenic substrate
- Morphologic hypertrophy variants: asymmetric septal; concentric; midcavity; apical
- LVH evolves over time, typically manifests in adolescence

Pathophysiology

- Subaortic outflow obstruction: narrowed tract 2° hypertrophied septum + systolic anterior motion (SAM) of ant. MV leaflet (may be fixed, variable or nonexistent) and papillary muscle displacement. Gradient (▽) worse w/ ↑ contractility (digoxin, β-agonists, exercise, PVCs), ↓ preload or ↓ afterload.

P.1-32

- Mitral regurgitation: due to SAM (mid-to-late, post.-directed regurg. jet) and/or abnl mitral leaflets and papillary muscles (pansystolic, ant.-directed regurg. jet)
- Diastolic dysfunction: ↑ chamber stiffness + impaired relaxation
- Ischemia: small vessel dis., perforating artery compression (bridging), ↓ coronary perfusion
- Syncope: Δs in load-dependent CO, arrhythmias

Clinical manifestations (70% asymptomatic at dx)

- **Dyspnea** (90%): due to ↑ LVEDP, MR, and diastolic dysfunction
- **Angina** (25%) even w/o epicardial CAD; microvasc. dysfxn (*NEJM* 2003;349:1027)
- **Arrhythmias** (AF in 20-25%; VT/VF) → palpitations, syncope, sudden cardiac death

Physical exam

- Sustained PMI, S_2 paradoxically split if severe outflow obstruction, ⊕ S_4 (occ. palpable)
- **Systolic murmur:** crescendo-decrescendo; LLSB; ↑ **w/ Valsalva** & standing (↓ preload)
- ± mid-to-late or holosystolic murmur of MR at apex
- Bifid carotid pulse (brisk rise, decline, then 2nd rise); JVP w/ prominent *a* wave
- Contrast to AS, which has murmur that ↓ w/ Valsalva and ↓ carotid pulses

Diagnostic studies

- CXR: cardiomegaly (LV and LA)
- ECG: LVH, anterolateral and inferior pseudo-Qw, ± apical giant TWI (apical variant)
- Echo: no absolute cutoffs for degree of LVH but septum/post. wall ≥1.3 suggestive, as is septum >15 mm; other findings include dynamic outflow obstruction, SAM, MR
- MRI: hypertrophy + patchy delayed enhancement (useful for dx & prog) (*Circ* 2015;132:292)
- Cardiac cath: subaortic pressure ▽ *Brockenbrough sign* = ↓ pulse pressure post-PVC (in contrast to AS, in which pulse pressure ↑ post-PVC)
- ? Genotyping for family screening, but pathogenic mutation ID'd in <½ (*Circ* 2011;124:2761)

Treatment (*Circ* 2011;124:e783 & 2012;125:1432; *Lancet* 2013;381:242; *EHJ* 2014;35:2733)

- Heart failure

  ⊖ **inotropes/chronotropes:** nonvasodilating βBs, CCB (verapamil), disopyramide

  Careful use of diuretics, as may further ↓ preload. Vasodilators only if systolic dysfxn. Avoid digoxin.

  If sx refractory to drug Rx + *obstructive* physiology (▽ >50 mmHg):

  (a) Surgical myectomy: long-term ↓ symptoms in 90% (*Circ* 2014;130:1617)

  (b) Alcohol septal ablation (*Circ* CV *Interv* 2011;4;256; *JACC* 2011;58:2322): gradient ↓ by ˜80%, only 5-20% remain w/ NYHA III-IV sx; 14% require repeat ablation or myectomy. Good alternative for older Pts, multiple comorbidities. Complic: transient (& occ. delayed) 3° AVB w/ 10-20% req. PPM; VT due to scar formation.

  No clear benefit of dual-chamber pacing (*JACC* 1997;29:435; *Circ* 1999;99:2927)

  If refractory to drug therapy and there is *nonobstructive* pathophysiology: transplant
- Acute HF: can be precip. by dehydration or tachycardia; Rx w/ fluids, βB, phenylephrine
- AF: rate control with βB, maintain SR with disopyramide, amiodarone; low threshold to anticoagulate
- SCD: ICD (*JACC* 2003;42:1687). Risk factors: h/o VT/VF, ⊕ FHx SCD, unexplained syncope, NSVT, ↓ SBP or rel HoTN (↑ SBP <20 mmHg) w/ exercise, LV wall ≥30 mm, extensive MRI delayed enhancement. EPS *not* useful. Risk 11%/y if h/o VT/VF, 4%/y if highrisk w/o h/o VT/VF (*JAMA* 2007;298:405).
- Counsel to avoid dehydration, competitive sports & extreme exertion
- Endocarditis prophylaxis not recommended (*Circ* 2007;16:1736)
- First-degree relatives: periodic screening w/ echo, ECG (as timing of HCM onset variable). Genetic testing if known mutation. ? CCB for preclinical HCM (*JACC* HF 2015;3:180).

RESTRICTIVE CARDIOMYOPATHIES (RCM)

Definition (*Circ* 2006;113:1807)

- Impaired ventricular filling with ↓ compliance in nonhypertrophied, nondilated ventricles; normal or ↓ diastolic volumes, normal or near-normal EF; must r/o pericardial disease

Amyloidosis (*Circ* 2011;124:1079 & 2012:126:1286)

- Extracellular deposition of misfolded proteins in a variety of organs (eg, heart, kidney, liver, autonomic nervous system; deposition leads to morbidity & mortality)
- Age at presentation ˜60 y; ♂: ♀ 3:2
- AL (primary; MM, light-chain, MGUS, WM): multiorgan disease (˜50% cardiac)
- ATTR (familial; mutation in transthyretin, TTR; *Circ* 2012;126:1286)

  V122I variant → 2.6× ↑ HF risk; 10% carriage in blacks >65 y w/ HF (*JACC* 2006:47:1724)

  V30M variant seen in European & Japanese

  T60R variant in Europeans, autonomic + peripheral neuropathy common

- SSA (senile; normal TTR): typically presents at age >70 y, prevalence >5% beyond age 80, ♂ >> ♀ (50:1), heart-only

- Workup

  ECG: ↓ QRS amplitude in AL (50%), pseudoinfarct pattern (Qw), AVB (10-20%), hemiblock (20%), BBB (5-20%)

  Echo: biventricular wall thickening (*yet* w/ *low voltage on* ECG), granular sparkling texture (30%), biatrial enlargement (40%), thickened atrial septum, valve thickening (65%), diastolic dysfxn, small effusions

  Normal voltage & septal thickness has NPV ˜*90%*

  Lab: SPEP, UPEP, serum free light chain ratio (<0.25 or >1.65 κ-to-λ ratio) 91% Se for AL amyloid (*Clin Chem* 2005;51:878)

  MRI: diffuse subendo late gado enhance, ˜90% Se/Sp vs bx (*JACC* 2008;51:1022)

  (99m)Tc-pyrophosphate PET: ↑ tracer retention in ATTR >> AL differentiates cardiac amyloid subtypes (*Circ Imaging* 2013;6:195)

  Cardiac bx: gold standard (˜100% Se due to widespread amyloid distrib) and permits subtyping of precursor protein. Abd fat pad bx 70% sensitivity for AL.

- Treatment: judicious loop diuretics often only tolerated Rx avoid digoxin (↑ toxicity w/ binding fibrils) and CCB (⊖ inotrope)

  βB or ACEI often poorly tolerated b/c of HoTN

  cardiac tx usually contraindic. b/c extracardiac involvement, but isolated cardiac AL amyloid combined heart/auto stem cell tx yields survival ≈ other RCM (*JHLT* 2014;33:149)

  LVADs not appropriate b/c small restricted LV and frequent RV dysfunction

- Prognosis (median survival after HF dx): AL <12 mo, ATTR ˜30 mo, SSA ˜60 mo

Sarcoidosis

- Noncaseating, granulomatous disorder that can involve any organ
- Recognized cardiac disease in ˜5% of those w/ systemic sarcoid, but imaging & autopsy data show myocardial involvement in >50%
- LV dysfxn (DCM ≥ RCM); MR can be due to involvement of papillary muscles
- ECG: AVB (75%), can be high grade; RBBB (20-60%); atrial & vent. arrhythmias
- Cardiac MRI: T2-imaging and early gadolinium detect acute inflammation (edema), nontransmural patchy delayed gado enhancement, particularly in basal and/or midventricular septum detects fibrosis/scar from chronic disease and predicts prognosis (⊕ LGE → 31× risk for adverse cardiac events; *JACC Imaging* 2013;6:501)
- Echo: regional WMA (particularly basal septum) with thinning or mild hypertrophy
- Nuclear imaging: thallium perfusion defects in a noncoronary distribution; gallium uptake in areas of active inflammation can guide steroid Rx; PET: ↑ FDG uptake in areas of active inflammation
- Cardiac bx w/ low yield as granulomas patchy
- Treatment: steroids are standard although have not been evaluated in RCTs; 47% of Pts w/ AV conduction disease improved w/ steroids (*Can J Cardiol* 2013;29:1034) and retrospective studies suggest ↓ mortality. For steroid-sparing or intolerance, consider MTX, AZA, chloroquine or anti-TNF drugs. Low threshold for PPM-ICD.

Hemochromatosis

- In middle-aged men (espec Northern European)
- 15% p/w cardiac sx, typically HF and conduction disturbances
- Cardiac MRI: myocardial T2* is reduced (<20 ms) in iron overload disorders and enables tracking of response to Rx
- Treatment w/ phlebotomy or, in one report, chelation has been associated with reversal of LV dysfunction (*JACC* 1986;8:436)

Other etiologies (*Circ* 2005;112:2047 & *JACC* 2010;55:1769)

- **Myocardial processes**

  Autoimmune (scleroderma, polymyositis-dermatomyositis)

  Infiltrative diseases (see primary entries for extracardiac manifestations, Dx, Rx)

  Storage diseases: Gaucher's, Fabry, Hurler's, glycogen storage diseases

  Diabetes mellitus

- **Endomyocardial processes**

  Chronic eosinophilic: Löffler's endocarditis (temperate climates; ↑ eos; mural thrombi that embolize); endomyocardial fibrosis (tropical climates; var. eos; mural thrombi; *NEJM* 2008;359:43); treat for heart failure, steroids early, anticoagulation for thrombus

  Toxins: radiation (also p/w constrictive pericarditis, valvular dis, ostial CAD), anthracyclines

  Serotonin: carcinoid, serotonin agonists, ergot alkaloids

  Metastatic cancer

Pathology & pathophysiology

- Path: normal or ↑ wall thickness ± infiltration or abnormal deposition
- ↓ myocardial compliance → nl EDV but ↑ EDP → ↑ systemic & pulm. venous pressures
- ↓ ventricular cavity size → ↓ SV and ↓ CO

Clinical manifestations (*Circ* 2000;101:2490)

- **Right-sided > left-sided heart failure** w/ peripheral edema ± ascites > pulmonary edema
- **Diuretic "refractoriness"**
- **Thromboembolic events**
- Poorly tolerated tachyarrhythmias; VT → syncope/sudden cardiac death

Physical exam

- ↑ JVP, ± Kussmaul's sign (JVP ↑ w/ inspiration, classically seen in *constrictive pericarditis*)
- Cardiac: ± S_3 and S_4 (usually absent in amyloid b/c atrial dysfxn), ± murmurs of MR and TR

- Congestive hepatomegaly, ± ascites and jaundice, peripheral edema

Diagnostic studies

- CXR: normal ventricular chamber size, enlarged atria, ± pulmonary congestion
- ECG: low voltage, pseudoinfarction pattern (Qw), ± arrhythmias
- Echo: ± symmetric wall thickening, biatrial enlarge., ± mural thrombi, ± cavity oblit. w/ diast dysfxn: ↑ early diast (E) and ↓ late atrial (A) filling, ↑ E/A ratio, ↓ decel. time
- Cardiac MRI/PET: may reveal inflammation or evidence of infiltration (but nonspecific)
- Initials labs: SPEP, UPEP & serum free light chains, Fe studies (transferrin sat, HFE mutation), BNP (typically higher in RCM than in constrictive pericarditis)
- Cardiac catheterization: atria: **M's** or **W's** (prominent *x* and y descents)

  Ventricles: **dip & plateau** (rapid ↓ pressure at onset of diastole, rapid ↑ to early plateau)

  Concordance of LV and RV pressure peaks during respiratory cycle (vs discordance in constrictive pericarditis; *Circ* 1996;93:2007)
- Endomyocardial biopsy if suspect infiltrative process; fat pad bx for amyloid
- Restrictive cardiomyopathy vs constrictive pericarditis: see "Pericardial Disease"

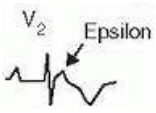
Treatment (in addition to Rx'ing underlying disease)

- Gentle diuresis. May not tolerate CCB or other vasodilators. Avoid digoxin in amyloid.
- Control HR (but can ↓ CO); maintain SR (helps filling). Digoxin ↑ arrhythmias in amyloid.
- Inotropes may have limited efficacy due to small ventricular cavity & preserved systolic fxn
- Anticoagulation (particularly with AF or low CO)
- Transplantation for refractory cases

OTHER CARDIOMYOPATHIES

Arrhythmogenic (right ventricular) cardiomyopathy (ACM, formerly ARVC)

- RV or biventricular (˜50%) or isolated LV (rare) dysfxn due to fatty infiltration and fibrous replacement (small amount of former normal variant) (*Lancet* 2009;373:1289)
- Due to mutations in desmosome (cell-cell coupling): eg, plakophilin 2, desmoglein, desmo-plakin; abnl Wnt signaling leads to myocytes → adipocytes
- Naxos syndrome (mutation in plakoglobin): wooly hair, palmar & plantar keratoses, ACM
- Clinical phases (*Circ* CV *Gen* 2015;8:437): (1) subclinical w/ nl imaging, but ↑ risk of SCD;

  (2) abnl ventricular fxn on imaging, sx ventricular arrhythmias (VT w/ LBBB morphology w/ superior axis), but no HF; (3) RV failure; (4) ? LV failure
- ECG: ± RBBB, TWI V_1-V_3, ε wave 

- Dx w/ MRI

- Avoid bx as septum usually *not* involved (∴ high false ⊖ rate) and risk of perforation w/ free wall bx
- Major dx criteria (*EHJ* 2010;31:806): (1) regional RV akinesia/dyskinesia and ↑ RVEDV;

  (2) fibrous replacement of RV free wall; (3) TWI V_1-V_3, (4) ε wave
- Treatment (*Circ* 2015;132:441): usual HF Rx; EP study & ICD; VT ablation as needed

Ion channelopathies (CMP despite lack of structural abnl; *Circ* 2006;113:1807)

- Defective ionic channel proteins lead to abnl cell membrane transit of Na and K ions
- Disorders include: LQTS, short-QT syndrome (SQTS), Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia (CPVT)

LV noncompaction (LVNC; *JACC* 2015;66:578)

- Prominent trabeculae w/ deep intertrabecular recesses due to intrauterine arrest of compaction of loose interwoven myocardial meshwork
- Debated whether distinct genetic CMP vs morphological trait of other CMPs
- Clinical: HF, atrial and/or vent arrhythmias, cardioembolic events
- Dx w/ MRI > echo; >2:1 ratio of noncompacted to compacted myocardium at end-systole, thickened LV wall and prominent deep trabeculae
- Usual HF Rx; low threshold to anticoagulate

VALVULAR HEART DISEASE

AORTIC STENOSIS (AS)

Etiology

- **Calcific:** predominant cause in Pts >70 y; risk factors include HTN, ↑ chol., ESRD
- **Congenital** (ie, bicuspid AoV w/ premature calcification): cause in 50% of Pts <70 y
- **Rheumatic heart disease** (AS usually accompanied by AR and MV disease)
- AS mimickers: subvalvular (HCMP subAo membrane) or supravalvular stenosis

Clinical manifestations (usually indicates AVA <1 cm^2 or concomitant CAD)

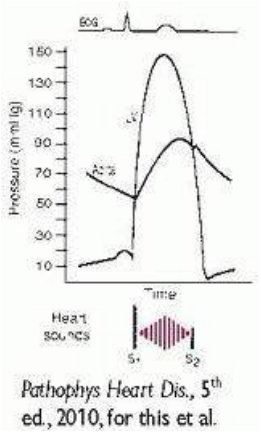
- **Angina:** ↑ O_2 demand (hypertrophy) + ↓ O_2 supply (↓ cor perfusion pressure) ± CAD
- **Syncope** (*exertional*): peripheral vasodil. w/ fixed CO → ↓ MAP → ↓ cerebral perfusion
- **Heart failure:** outflow obstruct + diastolic dysfxn → pulm. edema; espec If ↑ HR/AF (↓ LV fill.)
- Acquired vWF disease (~20% of sev. AS): destruction of vWF; GI angiodysplasia
- Natural hx: usually slowly progressive (AVA ↓ ~0.1 cm^2/y, but varies; *Circ* 1997;95:2262), until sx develop; mean survival based on sx: angina = 5 y; syncope = 3 y; CHF = 2 y

Physical exam

- **Midsystolic crescendo-decrescendo** murmur at **RUSB**, harsh, high-pitched, radiates to carotids, apex (holo-systolic = Gallavardin effect), ↑ w/ passive leg raise, ↓ w/ standing & Valsalva. In contrast, dynamic

outflow obstruction (HCM) ↓ w/ leg raise, ↑ w/ standing, Valsalva.

- Ejection click after S_1 sometimes heard with *bicuspid* AoV
- Signs of severity: *late-peaking* murmur, paradoxically split S_2 or inaudible A_2, small and delayed carotid pulse ("*pulsus parvus et tardus*"), LV heave, ⊕ S4 (occasionally palpable)



Pathophys Heart Dis., 5th ed., 2010, for this et al.

Diagnostic studies

- ECG: may see LVH, LAE, LBBB, AF (in late disease)
- CXR: cardiomegaly, AoV calcification, poststenotic dilation of ascending Ao, pulmonary congestion
- **Echo:** valve morphology, jet velocity, estim pressure gradient (∇) & calculate AVA, LVEF if concom severe AR: vel & ∇ may be ↑ than typical b/c of ↑ flow, but AVA calc valid if concom severe MR: vel & ∇ may be ↓ than typical b/c of ↓ flow, but AVA calc valid
- **Cardiac cath:** usually to r/o CAD (in ~½ of calcific AS); for hemodyn. if disparity between exam & echo: ✓ pressure gradient (∇) across AoV, calc AVA (underestim. if mod/sev AR)
- **Dobutamine challenge:** in cases with low flow, low ∇, and low LVEF, repeating echo (or cath) during low-dose dobutamine can differentiate:

Condition	Comment	SV	Jet Vel	∇	AVA
Afterload mismatch	Low EF 2° to severe AS; EF should ↑ post-AVR	≥20% ↑	↑	↑	no Δ
Pseudostenosis	Low AVA *artifact* of LV dysfxn	≥20% ↑	no Δ	no Δ	↑
Lack contractile reserve	EF prob. will *not* ↑ w/ AVR	no Δ	no Δ	no Δ	no Δ

Classification of Aortic Stenosis (*Circ* 2014;129:e521)

Stage	Sx	Severity	Max Jet Vel ($^m/_s$)	Mean Grad (mmHg)	AVA (cm^2)[a]	LVEF
n/a	N	Normal	1	0	3-4	nl
A	N	At risk	<2	<10	3-4	nl
B	N	Mild	2-2.9	<20	>1.5	nl
		Moderate	3-3.9	20-39	1-1.5	nl
C1		Severe	≥4	≥40	≤1.0	nl
	N	Very severe	≥5	≥60	≤0.8	nl
C2		Severe + ↓ EF	≥4	≥40	≤1.0	↓
D1		Severe	≥4	≥40	≤1.0	nl
D2	Y	Severe + low flow/∇ + ↓ EF[b]	<4	<40	≤1.0	↓
D3		Severe + low flow/∇ + nl EF[c]	<4	<40	≤1.0	nl

[a]AVA indexed to BSA <0.6 cm^2/m^2 also severe;

[b]DSE → max jet vel ≥4 & AVA ≤1.0;

[c]small LV w/ ↓ stroke vol.

Treatment (*Circ* 2014;129:e521 & *NEJM* 2014;371:744)

- Management decisions based on *symptoms*: once they develop AVR is needed. If asx, HTN can be cautiously Rx'd (probably best w/ ACEI/ARB rather than diuretics). Statins have not been proven to ↓ progression.
- **AVR**

  Indicated in: **sx severe AS** (ie, stage D1); **asx severe AS + EF <50%** (stage C2); or asx severe (stage C1) *and* undergoing other cardiac surgery.

  Reasonable if:

asx severe AS (stage C1) *but* either **sx or ↓ BP w/ exercise** (can *carefully* exercise asx AS to uncover sx, do *not* exercise sx AS) or **very severe**

sx severe w/ low flow/▽ w/ low EF & response to dobuta (stage D2) or normal EF but AS felt to be cause of sx (stage D3)

asx moderate AS (stage B) *and* undergoing cardiac surgery

- Transcatheter AoV replacement (TAVR, see below) indicated if surgical risk prohibitive or as reasonable alternative to surgery if high operative risk (STS predicted mortality 8-15%)
- Medical (if not AVR candidate or to temporize): careful diuresis prn, control HTN, maintain SR; digoxin if ↓ EF & HF or if AF; *avoid* venodilators (nitrates) & ⊖ inotropes (βB/CCB) if severe; avoid vigorous physical exertion once AS mod-severe; ? nitroprusside if p/w CHF w/ sev. AS, EF <35%, CI <2.2, & nl BP (*NEJM* 2003;348:1756)
- IABP: stabilization, bridge to surgery
- Balloon AoV valvotomy (BAV): 50% ↑ AVA & ↓ peak ▽, *but* 50% restenosis by 6-12 mo & ↑ risk of peri-PAV stroke/AR (*NEJM* 1988;319:125), ∴ bridge to AVR or palliation

TAVR (transcatheter AoV replacement)

- Catheter-based technique for replacing diseased AoV with bioprosthetic valve
- Valves: balloon-expandable (Edwards SAPIEN) or self-expanding (Medtronic CoreValve); balloon-expandable w/ less AR, less redo, less need for PPM (*JAMA* 2014;311:1503)
- Approaches: primarily retrograde via percutaneous transfemoral access; also retrograde via axillary artery or ascending aorta (via small sternotomy & aortotomy); alternatively transapical via direct LV apical puncture and antegrade implantation through small thoracotomy (if severe PAD or heavily calcified ascending Ao & arch)
- Periprocedural: local anesthesia w/ conscious sedation or general anesthesia; RV pacing (to decrease SV during deployment); TEE to guide placement
- Peri- & postprocedural complications: low CO, annular rupture or coronary occlusion (both rare), local vascular complications, paravalvular leaks & heart block (see below)
- ASA lifelong + clopidogrel × 6 mo
- Outcomes

  in nonoperative Pts vs med Rx: 44% ↓ mortality, but still ~20% annual mortality in TAVR group illustrating comorbidities in this population (*NEJM* 2012;366:1696; *JACC* 2014;63:1972)

  high-risk operative Pts vs surg AVR (*NEJM* 2012;366:1686 & 2014;370:1790) postop ≈ sx & hemodynamics mortality ≈ (balloon-expandable) or 26% ↓ (self-expanding) w/ TAVR vs surgery ↑ vasc complic; ↑ early risk of stroke/TIA w/ balloon-expandable heart block requiring PPM in ~20% w/ self-expanding; paravalvular leaks in ~7% prelim data in low-risk Pts shows lower mortality & stroke with TAVR (*JACC* 2015;65:2184)

AORTIC REGURGITATION (AR)

Etiology (*Circ* 2006;114:422)

- **Valve disease** (43%)

  rheumatic heart disease (usually mixed AS/AR and concomitant MV disease)

  bicuspid AoV: natural hx: ⅓→ normal, ⅓ → AS, 1/6 → AR, 1/6 → endocarditis → AR **infective endocarditis**

valvulitis: RA, SLE; anorectics (fen/phen) & other serotoninergics (*NEJM* 2007;356:29,39), XRT

- **Root disease** (57%)

  HTN

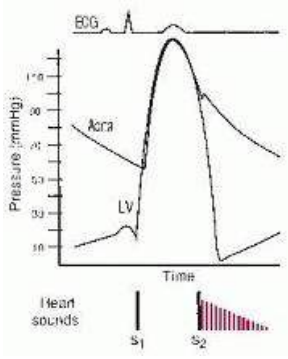
  aortic aneurysm or dissection, annuloaortic ectasia, Marfan syndrome

  aortic inflammation: giant cell, Takayasu's, ankylosing spond., reactive arthritis, syphilis

Clinical manifestations

- Acute: sudden ↓ forward SV and ↑ LVEDP (noncompliant ventricle) → pulmonary edema ± hypotension and cardiogenic shock
- Chronic: clinically silent while LV dilates (to ↑ compliance to keep LVEDP low) more than it hypertrophies → chronic volume overload → LV decompensation → CHF
- Natural hx: *variable* progression (unlike AS, can be fast or slow); once decompensation begins, prognosis poor w/o AVR (mortality ~10%/y)

Physical exam



- **Early diastolic decrescendo murmur at LUSB** (RUSB if dilated Ao root); ↑ w/ sitting forward, expir, handgrip; severity of AR ∝ duration of murmur (except in acute and severe late); *Austin Flint murmur:* mid-to-late diastolic rumble at apex (AR jet interfering w/ mitral inflow)
- **Wide pulse pressure** due to ↑ stroke volume, hyper-dynamic pulse → many of classic signs (see table); pulse pressure narrows in late AR with ↓ LV fxn; bisferiens (twice-beating) arterial pulse
- PMI diffuse and laterally displaced; soft S_1 (early closure of MV); ± S_3 (≠ ↓ EF but rather just volume overload in AR)

Classic Eponymous Signs in Chronic AR (*South Med J* 1981;74:459)

Sign	Description
Corrigan's pulse	“water hammer” pulse (ie, rapid rise/fall or distention/collapse)
Hill's sign	(popliteal SBP - brachial SBP) >60 mmHg
Duroziez's sign	to-and-fro murmur heard over femoral artery w/ light compression

Pistol shot sounds	pistol shot sound heard over femoral artery
Traube's sound	double sound heard over femoral artery when compressed distally
de Musset's sign	head-bobbing with each heartbeat (low Se)
Müller's sign	systolic pulsations of the uvula
Quincke's pulses	subungual capillary pulsations (low Sp)

Diagnostic studies

- ECG: can see LVH, LAD, abnl repol; CXR: cardiomegaly ± ascending Ao dilatation
- **Echo:** severity of AR (in addition to parameters below, severe AR requires holodia-stolic flow reversal in proximal abdominal Ao); LV size & fxn (chronic severe AR requires LV dilatation; LV dysfxn = EF <50% or LV end-syst. diam. [LVESD] >50 mm)
- Cardiac MR if TTE not sufficiently informative

Classification of Aortic Regurgitation

Severity	Regurg. fraction (%)	Jet width (% of LVOT)	ERO (cm^2)	Angio*
Mild	<30	<25	<0.1	1+
Moderate	30-49	25-64	0.1-0.29	2+
Severe	≥50	≥65	≥0.3	3/4+

*1+ = incomplete LV opac.; 2+ = opac. <Ao root & clears 1 beat; 3+ = LV = Ao root opac.; LV > Ao root opac.

Treatment (*Circ* 2014;129:e521)

- Acute decompensation (consider ischemia and endocarditis as possible precipitants):
  surgery usually urgently needed for acute severe AR, which is poorly tolerated by LV IV afterload reduction (nitroprusside) and inotropic support (dobutamine) ± chronotropic support (↑ HR → ↓ diastole → ↓ time for regurgitation) pure vasoconstrictors and IABP contraindicated
- In chronic AR, management decisions based on LV *size and fxn* (and before sx occur)
- **Surgery** (AVR, replacement or repair if possible):
  severe and **sx** (if equivocal, consider stress test)
  asx *and* either **EF ≤50%** or **LV dilation** (LVESD >50 mm) or undergoing cardiac surg
- Transcatheter AoV replacement (TAVR) being explored (*JACC* 2013;61:1577)

- Medical therapy: **vasodilators** (nifedipine, ACEI/ARB, hydralazine) if severe AR w/ sx or LV dysfxn & Pt not operative candidate or to improve hemodynamics before AVR; no clear benefit on clinical outcomes or LV fxn when used to try to prolong compensation in asx severe AR w/ mild LV dilation & nl LV fxn (*NEJM* 2005;353:1342)

MITRAL REGURGITATION (MR)

Etiology (*Lancet* 2009;373:1382; *NEJM* 2010;363:156)

- **Primary** (degeneration of valve apparatus)

  leaflet abnl*:* myxomatous (MVP), endocarditis, calcific RHD, valvulitis (collagen-vascular disease), congenital, anorectic drugs, XRT

  chordae tendineae rupture: myxomatous, endocarditis, spontaneous, trauma

  papillary muscle dysfxn b/c of ischemia or *rupture* during MI [usu. posteromedial papillary m. (supplied by PDA only) vs anterolateral (suppl. by diags & OMs)]

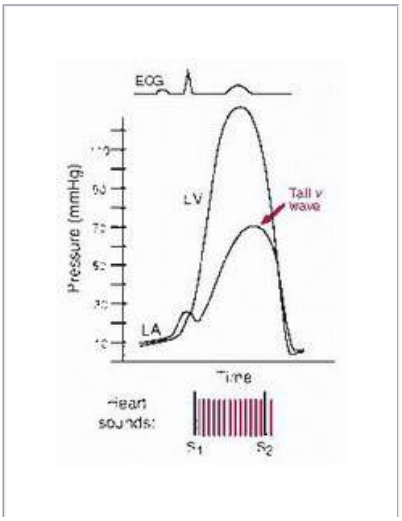
- **Secondary (functional):** inferoapical papillary muscle displacement due to ischemic LV remodeling or other causes of DCM (*JACC* 2015;65:1231)

Clinical manifestations

- Acute: **pulmonary edema**, hypotension, cardiogenic shock (*NEJM* 2004;351:1627)
- Chronic: typically asx for yrs, then as LV fails → progressive DOE, fatigue, AF, PHT
- Prognosis: 5-y survival w/ medical therapy is 80% if asx, but only 45% if sx

Physical exam

- **High-pitched, blowing, holosystolic murmur at apex;** radiates to axilla; ± thrill; ↑ w/ handgrip (Se 68%, Sp 92%), ↓ w/ Valsalva (Se 93%) (*NEJM* 1988;318:1572) ant. leaflet abnl → post. jet heard at spine post. leaflet abnl → ant. jet heard at sternum
- ± diastolic rumble b/c ↑ flow across valve
- Lat. displ. hyperdynamic PMI, obscured S_1, widely split S_2 (A_2 early b/c ↓ LV afterload, P_2 late if PHT); ± S_3
- Carotid upstroke brisk (vs diminished and delayed in AS)



Diagnostic studies (*NEJM* 2005;352:875)

- ECG: may see LAE, LVH, ± atrial fibrillation
- CXR: dilated LA, dilated LV, ± pulmonary congestion
- **Echo:** MV anatomy (ie, etiol); MR severity: jet area (can underestimate eccentric jets), jet width at origin (vena contracta) or effective regurgitant orifice (ERO; predicts survival); LV fxn (EF should be *supranormal* if compensated, [EF <60% w/ sev. MR = LV dysfxn); TEE if TTE inconclusive or pre/intraop to guide repair vs replace
- Cardiac MR if TTE not sufficiently informative
- **Cardiac cath:** prominent PCWP *c-v* waves (not spec. for MR), LVgram for MR severity & EF

Classification of Primary Mitral Regurgitation

Severity	**Regurg. fraction**	**Jet area** (% of LA)	**Jet width** (cm)	**ERO** (cm^2)	**Angio***
Mild	<30%	<20	<0.3	<0.2	1+
Moderate	30-49%	20-40	0.3-0.69	0.2-0.39	2+
Severe†	≥50%	>40	≥0.70	≥0.40	3/4+

*1+ = LA clears w/ each beat; 2+ = LA does not clear, faintly opac. after several beats; 3+ = LA & LV opac. equal.

†For secondary MR, because ERO underestimated & likely progressive LV dysfxn, ERO ≥0.20 is severe

Treatment (*Circ* 2014;129:e521)

- Acute decompensation (consider ischemia and endocarditis as precipitants) IV afterload reduction (nitroprusside), ± inotropes (dobuta), IABP, avoid vasoconstrictors *surgery* usually needed for acute severe MR as prognosis poor w/o (*JAMA* 2013;310:609)
- **Surgery** (repair [preferred if feasible] vs replacement w/ preservation of mitral apparatus)

  for **severe** *primary* MR indicated if **sx & EF >30%** or if **asx & either EF 30-60% or LV sys. diam. ≥40 mm** MV *repair* reasonable if asx & either EF >60% + LVESD <40 mm or new AF or PHT if AF, maze procedure or pulm vein isolation → ↓ AF recurrence, Ø Δ stroke; consider for sx cntl or if planning no anticoag (*NEJM* 2015;372:1399)

  for **severe** *secondary* MR*:* consider if NYHA III-IV; replacement results in more durable correction than repair but no difference in clinical outcomes (*NEJM* 2014;370:23)
- In Pts undergoing CABG w/ mod-sev fxnal MR, annuloplasty ↓ MR but longer surgery, ↑ neurologic events, & no impact on fxnal status or mortality (*NEJM* 2014;371:2178)
- Percut. MV repair (*Circ* 2014;130:1712): edge-to-edge clip less effective than surgery but consider for

sev. sx nonoperative Pt (*NEJM* 2011;364:1395); perc valve under study (*JACC* 2014;64:1814)

- Medical: Ø clinical benefit in asx Pts; βB preserve LV fxn (*JACC* 2012;60:833); if sx but not operative candidate ↓ preload (↓ HF and MR by ↓ MV orifice): diuretics, nitrates (espec if ischemic/fxnal MR); if LV dysfxn: ACEI, βB, ± BiV pacing; maintain SR

MITRAL STENOSIS (MS)

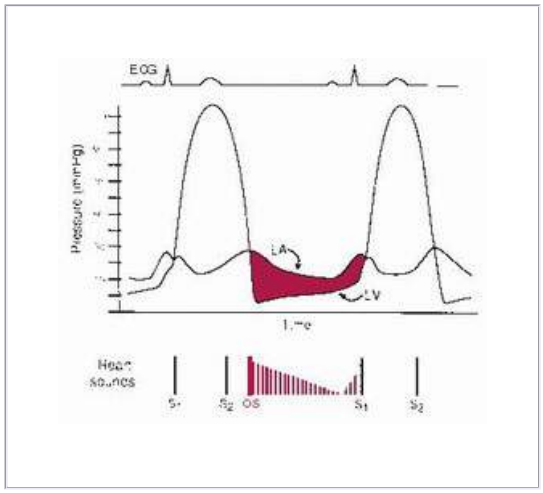
Etiology (*Lancet* 2012;379:953)

- **Rheumatic heart disease** (RHD): *fusion of commissures* → "fish-mouth" valve from autoimmune rxn to β strep infxn; seen largely in developing world today
- **Mitral annular calcification** (MAC): encroachment upon leaflets → functional MS
- Congenital, infectious endocarditis w/ large lesion, myxoma near MV, thrombus
- Valvulitis (eg, SLE, amyloid, carcinoid) or infiltration (eg, mucopolysaccharidoses)

Clinical manifestations (*Lancet* 2009;374:1271)

- **Dyspnea and pulmonary edema** (if due to RHD, sx usually begin in 30s) precipitants: exercise, fever, anemia, volume overload (incl. pregnancy), tachycardia, AF
- **Atrial fibrillation:** onset often precipitates heart failure in Pts w/ MS
- **Embolic events:** commonly cerebral, espec in AF or endocarditis

- Pulmonary: hemoptysis, frequent bronchitis (due to congestion), PHT, RV failure
- Ortner's syndrome: hoarseness from LA compression of recurrent laryngeal nerve



Physical exam

- **Low-pitched mid-diastolic rumble at apex** w/ presystolic accentuation (if not in AF); best heard in L lat decubitus position during expiration, ↑ w/ exercise; severity proportional to *duration* (not intensity) of murmur
- **Opening snap** (high-pitched early diastolic sound at apex) from fused leaflet tips; MVA proportional to S_2-OS interval (tighter valve → ↑ LA pressure → shorter interval)
- Loud S_1 (unless MV calcified)

Diagnostic studies

- ECG: **LAE** ("P mitrale"), ± AF, ± RVH
- CXR: **dilated LA** (straightening of left heart border, double density on right, left mainstem bronchus elevation)
- **Echo:** estimate pressure gradient (▽), RVSP, valve area, valve echo score (0-16, based on leaflet mobility & thick., subvalvular thick., Ca^{++}); exer. TTE (to assess Δ RVSP and ▽) if sx & severity of MS at rest discrepant; TEE to assess for LA thrombus before PMV
- **Cardiac cath:** ▽ from simultaneous PCWP & LV pressures, calculated MVA; LA pressure tall *a* wave and blunted y descent; ↑ PA pressures

Classification of Mitral Stenosis

Stage	Mean ▽ (mmHg)	Pressure ½ time	MV area (cm^2)	PA systolic (mmHg)
Normal	0		4-6	<25
Mild-Mod	<5	100-149	1.6-2	<30
Severe	5-9	150-219	1.1-1.5	30-50
Very severe	≥10	≥220	≤1	>50

Treatment (*Circ* 2014;129:e521)

- Medical: Na restriction, cautious diuresis, βB, sx-limited physical stress
- Antibiotic Ppx recommended if h/o RHD w/ valvular disease for 10 y or until age 40
- Anticoag if: AF; prior embolism; LA thrombus; ? LA >55 mm or lg LA w/ spont contrast
- Mechanical intervention indicated if **heart failure sx w/ MVA ≥1.5;**
  reasonable if asx but very severe (MVA ≤1) and morphology favorable for PMBC; may consider PMBC if MVA >1.5 but hemodyn signif w/ exercise, or if asx but MVA ≤1.5 and new-onset AF
- **Percutaneous mitral balloon commissurotomy** (PMBC): preferred Rx if RHD; MVA doubles, ▽ ↓ by 50%; ≈ MVR *if* valve score <8, ≤ mild MR, Ø AF or LA clot
- Surgical (MV repair if possible, o/w replacement): consider in sx Pts w/ MVA ≤1.5 if PMV unavailable/contraindicated (mod. MR, LA clot), or valve morphology unsuitable
- Pregnancy: if NYHA class III/IV → PMV, o/w medical Rx w/ low-dose diuretic & βB

MITRAL VALVE PROLAPSE (MVP)

Definition and Etiology

- Billowing of MV leaflet ≥2 mm above mitral annulus in parasternal long axis echo view
- Leaflet redundancy from myxomatous proliferation of spongiosa of MV apparatus

- Idiopathic, familial and a/w connective tissue diseases (eg, Marfan's, Ehlers-Danlos)
- Prevalence 1-2.5% of gen. population, ♀ > ♂ (*NEJM* 1999;341:1), most common cause of MR

Clinical manifestations (usually asymptomatic)

- MR (from leaflet prolapse or ruptured chordae); infective endocarditis; embolic events
- Arrhythmias, rarely sudden cardiac death

Physical exam

- High-pitched, midsystolic click ± mid-to-late systolic murmur
- ↓ LV volume (standing) → click earlier; ↑ LV volume or afterload → click later, softer

Treatment

- Endocarditis prophylaxis no longer recommended (*Circ* 2007:116:1736)
- Aspirin or anticoagulation if prior neurologic event or atrial fibrillation

TRICUSPID REGURGITATION

- Primary etiol: rheumatic, CTD, radiation, IE, Ebstein's anomaly, carcinoid, tumors
- Fxnal etiol: RV and/or pulm HTN (may be 2° to L-sided dis.), RV dilation and/or infarct

- Assess based on severity TR, annular dilation, leaflet coaptation (*JACC* 2015;65:2331)
- Consider repair, annuloplasty or replacement for sx and severe TR (eg, ERO ≥ 0.40 cm^2)

PROSTHETIC HEART VALVES

Mechanical (60%)

- Bileaflet (eg, St. Jude Medical); tilting disk; caged-ball
- Very durable (20-30 y), but thrombogenic and ∴ require anticoagulation consider if age <˜60 y or if anticoagulation already indicated (*JACC* 2010;55:2413)

Bioprosthetic (40%)

- Bovine pericardial or porcine heterograft (eg, Carpentier-Edwards), homograft
- Less durable, but min. thrombogenic; consider if >˜70 y, lifespan <20 y or Ø anticoag
- If 50-69 y, 2× reop but ½ bleeding or stroke vs mech (*JAMA* 2014;312:1323 & 2015;313:1435)

Physical exam

- Normal: **crisp sounds**, ± soft murmur during forward flow (normal to have small ▽)
- Abnormal: regurgitant murmurs, absent mechanical valve closure sounds

Anticoagulation & antiplatelet therapy (*Circ* 2014;129:e521)

- Assess for *high-risk features:* prior thromboembolism, AF, EF<30-35%, hypercoagulable

- **Warfarin:** low-risk mech AVR: INR 2-3

  mech MVR or high-risk mech AVR: INR 2.5-3.5

  high-risk bioprosthetic: INR 2-3; for 1st 3 mo, reasonable in low-risk MVR, consider in low-risk AVR
- **ASA** (75-100 mg) for all prosthetic valves; avoid adding to warfarin if h/o GIB, uncontrolled HTN, erratic INR or >80 y
- If thrombosis, ↑ intensity (eg, INR 2-3 → 2.5-3.5; 2.5-3.5 → 3.5-4.5; add ASA if not on)

Periprocedural "Bridging" of Anticoagulation in Pts with Mechanical Valve(s)

AVR w/o risk factors	d/c warfarin 2-4 before surg; restart 12-24 h after surg
MVR or AVR w/ risk factors	Preop: d/c warfarin, start UFH when INR <2 4-6 h preop: d/c UFH; postop: restart UFH & warfarin ASAP

Procedures include noncardiac surgery, invasive procedures, and major dental work

Correction of overanticoagulation (*Circ* 2014;129:e521)

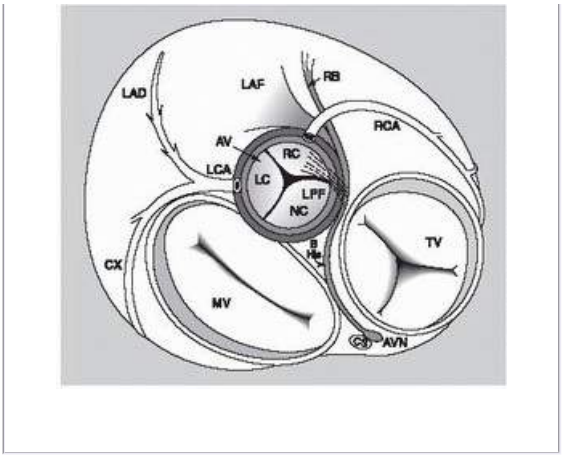
- Risk from major bleeding must be weighed against risk of valve thrombosis
- Not bleeding: if INR 5-10, withhold warfarin; if INR > 10 also give vit K 1-2.5 mg PO
- Bleeding: FFP or PCC ± low-dose (1 mg) vit K IV

Endocarditis prophylaxis: for all prosthetic valves (see "Endocarditis") Complications

- Structural failure (r/o endocarditis); mechanical valves: rare except for Bjork-Shiley; bioprosth: up to 30% rate w/in 10-15 y, mitral > aortic; consider TAVR (*JAMA* 2014;312:162)
- Paravalvular leak (r/o endocarditis); small *central* jet of regurg is normal in mech. valves
- Obstruction from thrombosis or pannus ingrowth: ✓ TTE, TEE, and/or fluoroscopy if ? clot significantly sx *pannus* ingrowth: remove w/ surgery

  thrombosis: surgery if L-sided valve & either severe sx or lg (? ≥0.8 cm) thrombus; lytic often *ineffective* for L-sided thrombosis & 12-15% risk of stroke; consider UFH ± lytic (? low-dose tPA via slow infusion, *JACC CV Imaging* 2013;6:206) if mild sx & small clot burden or poor surg candidate; lytic reasonable for R-sided
- Infective endocarditis ± valvular abscess and conduction system dis. (see "Endocarditis")
- Embolization (r/o endocarditis); risk ~ 1%/y w/ warfarin (vs 2% w/ ASA, or 4% w/o meds) mech MVR 2× risk of embolic events vs mech AVR (*Circ* 1994;89:635)
- Bleeding (from anticoag), hemolysis (espec w/ caged-ball valves or paravalvular leak)

HEART VALVES (superior view, *JAMA* 1976;235:1603)



AV = aortic valve

AVN = AV node

B His = bundle of His

CS = coronary sinus

Cx = circumflex artery

LAD = left anterior descending artery

LAF = left anterior fascicle

LCA = left coronary artery

LPF = left posterior fascicle

MV = mitral valve

RB = right bundle

RC/LC/NC = right/left/noncoronary cusp

RCA = right coronary artery

TV = tricuspid valve

CARDIOPULMONARY EXERCISE TESTING

Background, rationale, and measurements performed (*Circ* 2010;122:191)

- In exercise, to meet metabolic demands of active cells, need to ↑ effective ventilation, ↑ cardiac output, and ↓ pulmonary & systemic vascular resistance, ↑ O_2 extraction
- Dyspnea due to insufficient supply to or impaired uptake of O2 by skeletal muscle
- Ddx of dyspnea:

  impaired external respiration (ventilation & pulmonary gas exchange)

  impaired circulatory system (transport of O_2 and CO_2)

  impaired internal respiration (peripheral capillary gas exchange and O_2 utilization)
- Cardiorespiratory fitness predicts morbidity & mortality
- CPET is an individualized incremental exercise test that combines traditional cardiac stress test parameters: ECG, heart rate, BP quantification of O2 consumption ([V with dot above]O_2), CO_2 production ([V with dot

above]O_2), minute ventilation (V_E) if invasive (radial artery & PA cath): RAP, PAP, & PCWP; arterial & mixed venous sats can be coupled with cardiac imaging (eg, radionuclide ventriculography, TTE)

- Well tolerated even w/ advanced disease, 0.16% adverse event rate (*Circ* 2012:126:2465)

Indications for CPET

- Diagnose etiology of exercise intolerance or dyspnea by defining organ system limiting gas exchange (heart, pulm mechanical, pulm vasculature, muscles/mitochondria)
- Grade severity of advanced heart and lung diseases and predict prognosis

  Prioritize Pts for heart/lung transplantation, mechanical support:

  Heart transplant candidacy: peak [V with dot above]O_2 <14 ml/kg/min, <12 on βB, ± <50% predicted LVAD candidacy <12 ml/kg/min (*NEJM* 2001;345:1445)

  Determine whether to intervene on valvular disease, shunts/congenital heart disease
- To objectively measure responses to interventions (clinical trials, disability, rehabilitation)

Clinical relevance of measurement patterns

- RER (respiratory exchange ratio) = [V with dot above]CO_2/[V with dot above]O_2, indicator of volitional effort independent of chronotropic response (goal > 1.05)
- V_E/MVV (max voluntary vent): >70-80% indicates encroachment on pulm mechanical limit
- Peak [V with dot above]O_2: max aerobic capacity at peak exercise; indicator of cardiorespiratory fitness measured with metabolic cart but also represented by the Fick equation:

  [V with dot above]O_2 = (heart rate × stroke volume) × [(arterial - mixed venous) O_2 content]
- VAT (ventilatory anaerobic threshold): % of peak predicted [V with dot above]O_2 at which O_2 supply inadequate → anaerobic metabolism (normal value >40%); indep. of volitional effort, highly reproducible, and occurs at activity levels often assoc. w/ daily living. Low VAT reflects impaired O_2 delivery ± utilization but does not localize organ system responsible. In HFrEF, VAT<11 ml/kg/min assoc w/ 5× ↑ in 6-mo mortality (*Circ* 2002;106:3079).
- V_E/VCO_2 slope: ventilation required to exchange 1 L/min of CO_2 in addition, V_E/VCO_2 slope = constant / [P_aCO_2 × (1 - V_d/V_t)] high level (>36) especially seen in pulm vascular and/or RV dysfunction, where V/Q mismatch & ↓ pulm perfusion → ↑ V_d/V_t, and ↑ ventilatory drive → ↓ P_aCO_2

  high levels also indicate poor prognosis (*Circ* 2007;115:2410; *Circ* HF 2008;1:227)
- Exercise oscillatory vent: periodic breathing that reflects circul. delay (ie, low CO) relative to metab needs during exercise; assoc w/ 3× ↑ mort (*JACC* 2010;55:1814; *Circ* 2011;124:1442)
- mPAP/CO slope (serial measurements during exercise define the pulm artery pressure response to increased blood flow through the pulmonary circulation during exercise): mPAP = TPG + LAP mPAP/CO slope >3 indicates *either* abnl pulm vascular response to exercise *or* upstream transmission of high LAP (*Circ* 2013;128:1470), with TPG/CO (ie, PVR) that fails to fall and remains > 1.5 indicative of pulmonary vascular dysfunction and

  PCWP/CO slope >2 indicative of left-sided failure

- DPG (diastolic pulmonary gradient) = PAD - LAP; DPG >5-7 indicates pulm vasc disease and may be preferable to TPG (mPAP - LAP) for pulm vasc disease diagnosis b/c it is not significantly influenced by ΔLAP and CO (*Chest* 2013;143:758)

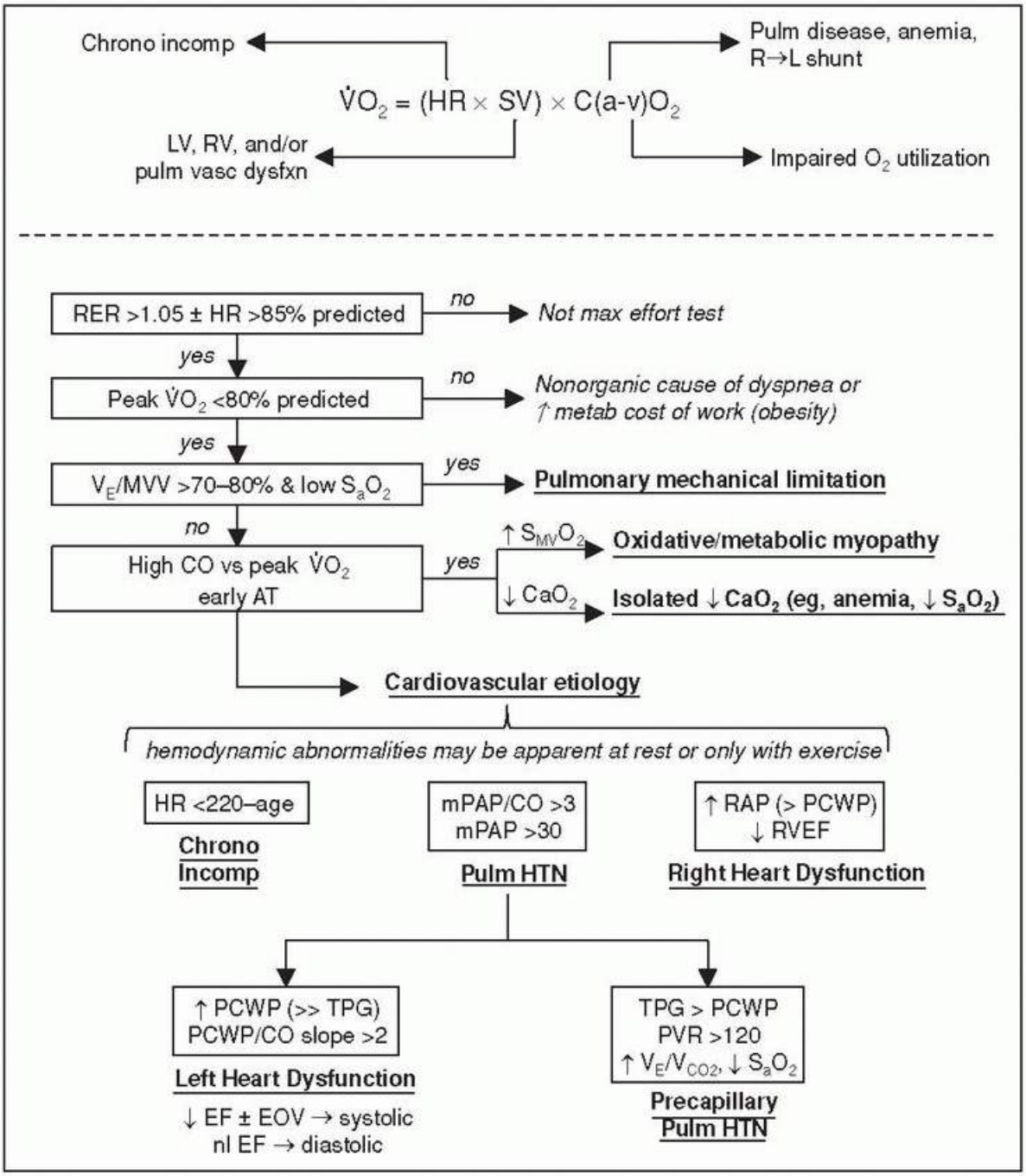


Figure 1-4 Approach to CPET

PERICARDIAL DISEASE

GENERAL PRINCIPLES

Anatomy

- 2-layered (parietal & visceral) tissue sac surrounding heart & proximal great vessels

Disease states

- Inflammation (w/ or w/o fluid accumulation) → pericarditis
- Fluid accumulation → effusion ± tamponade
- Decrease in compliance (sequela of inflammation) → constrictive pericarditis
- Tamponade and constriction characterized by increased ventricular interdependence

PERICARDITIS AND PERICARDIAL EFFUSION

Etiologies of Acute Pericarditis (*Lancet* 2004;363:717; *Curr Probl Cardiol* 2012;37:75)

Idiopathic (~90%)	Most presumed to be undiagnosed viral etiologies
Infectious (<5% can be confirmed infectious)	Viral: Coxsackie, echo, adeno, EBV, VZV, HIV, influenza Bacterial (from endocarditis, pneumonia or s/p cardiac surgery): *S. pneumococcus, N. meningitidis, S. aureus, Borrelia* (Lyme); TB Fungal: *Histo, Coccidio, Candida;* Parasitic: *Entamoeba, Echino*
Neoplastic (<10%)	*Common:* metastatic (lung, breast, lymphoma, leukemia, RCC) *Rare:* primary cardiac & serosal tumors (mesothelioma)
Autoimmune	Connective tissue diseases: SLE, RA, scleroderma, Sjögren's Vasculitides: PAN, Churg-Strauss, Wegener's Drug-induced: procainamide, hydralazine, INH, CsA
Uremia	~5-13% of Pts prior to HD; ~20% occurrence in chronic HD Pts
Cardiovascular	Acute STEMI, late post-MI (Dressler's syndrome), but both rare in modern era; proximal AoD; chest trauma/postpericardiotomy
Radiation	>40 Gy to mediastinum; acute or delayed; may be transudative
Effusions w/o pericarditis	HF, cirrhosis, nephrotic syndrome, hypothyroidism, amyloidosis Transudative

Clinical manifestations (*NEJM* 2014;371:2410)

- **Pericarditis:** retrosternal chest pain that is pleuritic, positional (↓ by sitting forward), radiates to trapezius; may be *absent* in TB, neoplastic, post-XRT and uremic pericarditis; ± fever; ± s/s of systemic etiologies
- **Effusion:** ranges from asx to tamponade (see below)

Physical exam

- **Pericarditis:** multiphasic **friction rub** best heard at LLSB w/ diaphragm of stethoscope. Notoriously variable and evanescent leathery sound w/ up to 3 components: atrial contraction, ventricular contraction, ventricular relaxation (*NEJM* 2012;367:e20).
- **Effusion:** distant heart sounds, dullness over left posterior lung field due to compressive atelectasis from

pericardial effusion (Ewart's sign)

Diagnostic studies (*EHJ* 2004;25:587; *Circ* 2006;113:1622 & 2010;121:916)

- ECG: may show diffuse STE (*concave up*) & PR depression (except in aVR: ST ↓ & PR ↑), TWI; classically and in contrast to STEMI, TWI do not occur until STs normalize Stages: (I) STE & PR ↓ ; (II) ST & PR normalize; (III) diffuse TWI; (IV) Tw normalize ECG may show evidence of large effusion w/ low voltage & electrical alternans (beat-to-beat Δ in QRS amplitude and/or axis due to swinging heart)
- CXR: if large effusion (>250 mL of fluid) → ↑ cardiac silhouette w/ "water-bottle" heart and epicardial halo
- **Echocardiogram:** presence, size, & location of *effusion;* presence of *tamponade physiology;* pericarditis itself w/o spec. abnl (∴ echo can be nl), although can see pericardial stranding (fibrin or tumor); can also detect LV/RV dysfxn (myocarditis ?)
- CT will reveal pericardial effusions, often appearing larger than on echocardiography
- CK-MB or troponin (⊕ in ~30%, *JACC* 2003;42:2144) if myopericarditis. Consider CRP/ESR.

Workup for effusion

- r/o infxn: usually apparent from Hx & CXR; ? value of ✓ acute and convalescent serologies
- r/o noninfectious etiologies: BUN, Cr, ANA, RF, HIV, screen for common malignancies
- Pericardiocentesis if suspect infxn or malignancy or large effusion (>2 cm) or recurrent ✓cell counts, TP, LDH, glc, Gram stain & Cx, AFB, cytology ADA, PCR for MTb, and specific tumor markers as indicated by clinical suspicion "exudate" criteria: TP >3 g/dL, TP_{eff}/TP_{serum} >0.5, LDH_{eff}/LDH_{serum} >0.6 or glc <60 mg/dL high Se (~90%) but *very low* Sp (~20%); overall low utility (*Chest* 1997;111:1213)
- Pericardial bx if suspicion remains for malignancy or TB

Treatment of pericarditis (*Circ* 2013;127:1723)

- High-dose **NSAID** (eg, ibuprofen 600-800 mg tid) or ASA (eg, 650-1000 mg tid) × 7-14 d then taper over wks; ASA preferred over NSAID in acute MI; consider PPI to ↓ risk of GIB
- Add **colchicine** 0.5 mg bid (qd if ≤70 kg) × 3 mo; ↓ risk of refractory or recurrent pericarditis by 50% (*NEJM* 2013;369:1522)
- Steroids (usually systemic; occ. intrapericardial) only for systemic rheum or autoimmune disorder, uremic, preg., contraindication to NSAID, or refractory idiopathic dis. Systemic steroids appear to ↑ rate of pericarditis recurrence (*Circ* 2008;118:667).
- Avoid anticoagulants (although no convincing data that ↑ risk of hemorrhage/tamponade)
- Infectious effusion → pericardial drainage (preferably surgically) + systemic antibiotics
- Acute idiopathic effusion self-limited in 70-90% of cases
- Recurrent pericarditis (*Circ* 2007;115:2739)

  risk factors: subacute, lg effusion/tamponade, T >38°C, lack of NSAID response after 7 d treatment: colchicine 0.5 mg bid × 6 mo (*Annals* 2011;155:409 & *Lancet* 2014;383:2232)
- Recurrent effusion: consider pericardial window (percutaneous vs surgical)

PERICARDIAL TAMPONADE

Etiology

- Any cause of pericarditis but espec **malignancy**, **uremia**, **idiopathic**, proximal aortic dissection with rupture, myocardial rupture
- Rapidly accumulating effusions most likely to cause tamponade as no time for pericardium to stretch (eg, to ↑ compliance) and accommodate ↑ intrapericardial fluid volume

Pathophysiology (*NEJM* 2003;349:684)

- ↑ intrapericardial pressure, compression of heart chambers, ↓ venous return → ↓ CO
- Diastolic pressures ↑ & equalize in all cardiac chambers → minimal flow of blood from RA to RV when TV opens → blunted y descent
- ↑ ventricular interdependence → pulsus paradoxus (pathologic exaggeration of nl physio) Inspiration → ↓ intrapericardial & RA pressures → ↑ venous return → ↑ RV size → septal shift to left. Also, ↑ pulmonary vascular compliance → ↓ pulm venous return. Result is ↓ LV filling → ↓ **LV stroke volume** & blood pressure.

Clinical manifestations

- **Cardiogenic shock** (hypotension, fatigue) **without pulmonary edema**
- Dyspnea (seen in ~85%) may be due to ↑ respiratory drive to augment venous return

Physical exam (*JAMA* 2007;297:1810)

- **Beck's triad** (present in minority of cases): **distant heart sounds**, ↑ **JVP**, **hypotension**
- ↑ JVP (76%) w/ blunted y descent
- Reflex tachycardia (77%), hypotension (26%; occasionally hypertensive), cool extremities
- **Pulsus paradoxus** (Se 82%, Sp 70%) = ↓ SBP ≥10 mmHg during inspiration

  ⊕ LR 3.3 (5.9 if pulsus >12), ⊖ LR 0.03

  Ddx = PE, hypovolemia, severe COPD, constriction (~⅓), RV infarct

  Can be absent if pre-existing ↑ LVEDP, arrhythmia, severe AI, ASD, regional tamponade
- Distant heart sounds (28%), ± pericardial friction rub (30%)
- Tachypnea but clear lungs

Diagnostic studies

- ECG: ↓ voltage (seen in 42%), electrical alternans (20%), ± signs of pericarditis
- CXR: ↑ cardiac silhouette (89%)
- **Echocardiogram:** ⊕ **effusion,** IVC plethora, **septal shift** with inspiration **diastolic collapse** of RA (Se 85%, Sp 80%) and/or RV (Se <80%, Sp 90%) **respirophasic** Δ's **in transvalvular velocities** (↑ across TV & ↓ across MV w/ inspir.) postsurgical tamponade may be localized and not easily visible
- Cardiac cath (right heart and pericardial): elevation (15-30 mmHg) and equalization of intrapericardial and

diastolic pressures (RA, RV, PCWP), blunted y descent in RA ↑ in stroke volume postpericardiocentesis = ultimate proof of tamponade if RA pressure remains elevated after drainage, may have effusive-constrictive disease (*NEJM* 2004;350:469) or myocardial dysfxn (eg, from concomitant myocarditis)

Treatment

- Volume (but be careful as overfilling can worsen tamponade) and ⊕ inotropes (avoid βB)
- Avoid vasoconstrictors as will ↓ stroke volume & potentially ↓ HR
- **Pericardiocentesis** (except if due to aortic or myocardial rupture, in which case consider removing just enough fluid to reverse PEA en route to emergent surgery)

CONSTRICTIVE PERICARDITIS

Etiology (*Circ* 2011;124:1270)

- Any cause of pericarditis (~1-2% incidence overall after acute pericarditis)
- Highest risk w/ **TB**, **bacterial**, **neoplastic**, connective tissue, postcardiac surgery
- **Viral/idiopathic**, as most common cause of pericarditis, also account for signif proportion

Pathophysiology

- Adhesion of visceral and parietal pericardial layers → rigid pericardium that limits diastolic filling of ventricles → ↑ systemic venous pressures
- Venous return is limited only after early rapid filling phase; ∴ rapid ↓ in RA pressure with atrial relaxation and opening of tricuspid valve and *prominent x and* y *descents*
- Kussmaul sign: JVP does not decrease with inspiration (↑ venous return with inspiration, but negative intrathoracic pressure not transmitted to heart because of rigid pericardium)

Clinical manifestations (*NEJM* 2011;364:1350)

- Right-sided > left-sided heart failure (systemic congestion > pulmonary congestion)

Physical exam

- ↑ **JVP** with **prominent y descent,** ⊕ **Kussmaul sign** (Ddx: tricuspid stenosis, acute cor pulmonale, RV failure and RV infarct, RCMP
- Hepatosplenomegaly, ascites, peripheral edema. Consider on Ddx of idiopathic cirrhosis.
- PMI usually not palpable, **pericardial knock**, usually no pulsus paradoxus

Diagnostic studies

- ECG: nonspecific, AF common (up to 33%) in advanced cases
- CXR: calcification (MTb most common), espec in lateral view (although not specific)
- Echocardiogram: ± thickened pericardium, "**septal bounce**" = abrupt displacement of septum during rapid filling in early diastole

- Cardiac catheterization: atria w/ **Ms** or **Ws** (prominent *x* and y descents) ventricles: **dip-and-plateau** or **square-root sign** (rapid ↓ pressure at onset of diastole, rapid ↑ to early plateau)

  discordance between LV & RV pressure peaks during respiratory cycle (*Circ* 1996;93:2007)

- CT or **MRI:** thickened pericardium (>4 mm; Se ~80%) w/ tethering (*Circ* 2011;123:e418)

Treatment

- Diuresis for intravascular volume overload; surgical pericardiectomy in advanced cases
- ? MRI able to predict reversibility with anti-inflammatory agents (*Circ* 2011;124:1830)

Constrictive Pericarditis vs Restrictive Cardiomyopathy

Evaluation	Constrictive pericarditis	Restrictive cardiomyopathy
Physical exam	⊕ Kussmaul sign Absent PMI ⊕ Pericardial knock	± Kussmaul sign Powerful PMI, ± S_3 and S_4 ± Murmurs of MR, TR
ECG	± Low voltage	Low voltage if infiltrative myopathy ± Conduction abnormalities
Echocardiogram	Respirophasic variation (25-40%): inspir. → ↑ flow across TV and ↓ flow across MV E′ (tissue velocity) nl/↑ (> 12) Expir. hepatic vein flow reversal Septal bounce during early diastole Normal wall thickness	<10% respirophasic variation Slower peak filling rate Longer time to peak filling rate E′ ↓ (<8 cm/sec) Inspir. hepatic vein flow reversal Biatrial enlargement ± ↑ wall thickness
CT/MRI	Thickened pericardium	Normal pericardium
NT-proBNP	Variable	Typically ↑ /↑ ↑ (*JACC* 2005;45:1900)
	Prominent *x* and *y* descents Dip-and-plateau sign	
Cardiac catheterization	LVEDP = RVEDP RVSP <55 mmHg (Se 90%, Sp 29%) RVEDP > ⅓ RVSP (Se 93%, Sp 46%) Discordance of LV & RV pressure peaks during respiratory cycle Systolic area index (ratio of RV to LV pressure-time area in inspir vs expir) >1.1 (Se 97%, Sp 100%)	LVEDP > RVEDP (esp. w/ vol.) RVSP >55 mmHg RVEDP <⅓ RVSP Concordance of LV & RV pressure peaks during respiratory cycle Systolic area index ≤1.1 (*JACC* 2008;51:315)

Endomyocardial biopsy	Usually normal	± Specific etiology of RCMP (fibrosis, infiltration, hypertrophy)

Vascular Disease

HYPERTENSION

Classification

Category	Systolic (mmHg)	Diastolic (mmHg)
Normal	<120	<80
Pre-HTN	120-139	80-89
Stage 1 HTN	140-159	90-99
Stage 2 HTN	≥160	≥100

Average ≥2 measurements >1-2 min apart. Confirm stage 1 w/in 1-4 wk; can Rx stage 2 immediately. ✓ q2y (if nl) or yearly (if pre-HTN). (*J Clin HTN* 2014;16:14)

Ambulatory Thresholds

Setting	Systolic (mmHg)	Diastolic (mmHg)
24-hr average	135	85
Day* (awake)	140	90
Night (asleep)	125	75

*Threshold of hypertension for home readings should be same as daytime ambulatory

Epidemiology (*Circulation* 2012;125:e2)

- Prevalence 33.5% in U.S. adults; >75 million affected (prevalence equal for men and women, highest in African American adults at 44%)
- ↑ Age → ↓ arterial compliance → systolic HTN
- Only 48% of patients with dx of HTN have adequate BP control

Etiologies

- **Essential** (95%): onset 25-55 y; ⊕ FHx. Unclear mechanism but ? additive microvasc renal injury over time w/

contribution of hyperactive sympathetics (*NEJM* 2002;346:913). Both genetic (*Nature* 2011;478:103) & environmental risk factors (Na, obesity, inactivity) Blacks more likely to be salt sensitive and have less activation of renin-angiotensin system, explaining preference for thiazides & CCB over ACEI or ARB

- **Secondary:** Consider if Pt <20 or >50 y or if sudden onset, severe, refractory HTN

Secondary Causes of Hypertension

Diseases		Suggestive findings	Initial workup
RENAL	**Renal parenchymal** (2-3%)	h/o DM, polycystic kidney disease, glomerulonephritis	CrCl, albuminuria See "Renal Failure"
	Renovascular (1-2%, qv) Athero (90%) FMD (10%, women) PAN, scleroderma	ARF induced by ACEI/ARB Recurrent flash pulm edema Renal bruit; hypokalemia (*NEJM* 2009;361:1972)	MRA (>90% Se & Sp, less for FMD), CTA, duplex U/S, angio, plasma renin (low Sp)
ENDO	**Hyperaldo or Cushing's** (1-5%)	Hypokalemia Metabolic alkalosis	See "Adrenal Disorders"
	Pheochromocytoma (<1%)	Paroxysmal HTN, H/A, palp.	
	Myxedema (<1%)	See "Thyroid Disorders"	TFTs
	Hypercalcemia (<1%)	Polyuria, dehydration, Δ MS	iCa
OTHER	**Obstructive sleep apnea** (qv)		
	Medications: OCP, steroids, licorice; NSAIDs (espec COX-2); Epo; cyclosporine		
	Aortic coarctation: ↓ LE pulses, systolic murmur, radial-femoral delay; abnl TTE, CXR		
	Polycythemia vera: ↑ Hct		

Standard workup (*J Clin HTN* 2014;16:14)

- Goals: (1) identify CV risk factors or other diseases that would modify prognosis or Rx;

  (2) reveal 2° causes of hypertension; (3) assess for target-organ damage
- History: CAD, HF, TIA/CVA, PAD, DM, renal insufficiency, sleep apnea, preeclampsia; ⊕ FHx for HTN; diet, Na intake, smoking, alcohol, prescription and OTC meds, OCP
- Physical exam: ✓ **BP in both arms**; funduscopic exam; BMI & waist circumference; cardiac (LVH, murmurs) including signs of HF, vascular (bruits, radial-femoral delay); abdominal (masses or bruits); neuro exam

- Testing: K, BUN, Cr, Ca, glc, Hct, U/A, lipids, TSH, urinary albumin:creatinine (if ↑ Cr, DM, or peripheral edema), ? renin, ECG (for LVH), CXR, TTE (eval for valve abnl, LVH)
- Ambulatory BP monitoring (ABPM): predictive of CV risk and ↑ Se & Sp for dx of HTN vs office BP (HTN 2005;46:156). Consider for suspected episodic or white coat HTN, resistant HTN, HoTN sx on meds, or suspected autonomic dysfxn. Rec by some guidelines to confirm HTN dx, so utilization may expand (*BMJ* 2011;342:d3621 & 343:d4891).

Complications of HTN

- *Each ↑ 20 mmHg* SBP *or 10 mmHg* DBP *→ 2× → CV complications* (*Lancet* 2002;360:1903)
- Neurologic: **TIA/CVA**, ruptured aneurysms, vascular dementia

- Retinopathy: stage I = arteriolar narrowing; II = copper wiring, AV nicking; III = hemorrhages and exudates; IV = papilledema
- Cardiac: **CAD**, **LVH**, **HF**, **AF**
- Vascular: aortic dissection, aortic aneurysm (HTN = key risk factor for aneurysms)
- Renal: proteinuria, **renal failure**

Treatment (*JAMA* 2014;311:507; *J Clin HTN* 2014;16:14; *JACC* 2015;65:1998)

- Goal: in general, <**140/90 mmHg**

  In elderly: data sparser, but benefit, albeit w/ less strict BP target (*NEJM* 2008;358:1887); thus, consider <150/90 mmHg if either (a) ≥80 y and w/o DM or CKD (ASH/ISH rec), or (b) ≥60 y (but no need to downtitrate if <140/90 & tolerating meds) (JNC 8 rec)

  In Pts w/ prior MI or stroke: reasonable to consider <130/80 (HTN 2015;65:1372)

  In Pts w/ DM and/or CKD: prior targets of <130/80 not supported by data (and harm if target <120; *NEJM* 2010;362:1575), but may consider if CKD & albuminuria for renal protection (ASH/ISH rec based on *NEJM* 1994;330:877)
- *Treatment results in 50% ↓ HF, 40% ↓ stroke, 20-25% ↓ MI* (*Lancet* 2014;384:591)
- **Lifestyle modifications** (each ↓ SBP ~5 mmHg) weight loss: goal BMI 18.5-24.9; aerobic exercise: ≥30 min exercise/d, ≥5 d/wk diet: rich in fruits & vegetables, low in saturated & total fat (DASH, *NEJM* 2001;344:3) sodium restriction: ≤2.4 g/d and ideally ≤1.5 g/d (*NEJM* 2010;362:2102) maintain adequate potassium intake through diet counseling (~120 mEq of dietary potassium) if no predisposition to hyperkalemia (*NEJM* 2007;356:1966)

  limit alcohol consumption: ≤2 drinks/d in ♂; ≤1 drink/d in ♀ & lighter-wt Pts avoid exacerbating exposures (eg, NSAID use)
- **Pharmacologic options** for HTN or pre-HTN w/ comorbidity (nb, pre-HTN w/o DM, CKD, CV disease, or other end organ dysfunction treated w/ lifestyle alone) **Pre-HTN:** ARB prevents onset of HTN, no ↑ in clinical events (*NEJM* 2006;354:1685) **HTN:** *choice of therapy controversial, concomitant disease and stage may help guide* Rx **uncomplicated:** CCB, ARB or ACEI, or thiazide (chlorthalidone preferred) are 1st line (*NEJM* 2009;361:2153); βB not 1st line (*Lancet* 2005;366:1545).

  For non-black Pts <60 y: reasonable to start w/ ARB or ACEI, then add CCB or thiazide if needed, and then add remaining class if still needed

  For black, elderly, and ? obese Pts (all of whom more likely to be salt sensitive): reasonable to start with

CCB or thiazide, then add either the other 1st choice class or ARB or ACEI if needed, and then all 3 classes if still needed

+CAD (*Circ* 2015;131:e435): ACEI or ARB (*NEJM* 2008;358:1547); ACEI+CCB superior to ACEI+thiazide (*NEJM* 2008;359:2417) or βB+diuretic (*Lancet* 2005;366:895); may require βB and/or nitrates for anginal relief; if h/o MI, βB ± ACEI/ARB ± aldo antag (see "ACS")

+HF: ACEI/ARB, βB, diuretics, aldosterone antagonist (see "Heart Failure")

+2° stroke prevention: ACEI (*Lancet* 2001;358:1033); ? ARB (*NEJM* 2008;359:1225)

+diabetes mellitus: ACEI or ARB; can also consider thiazide or CCB

+chronic kidney disease: ACEI or ARB (*NEJM* 1993;329:1456 & 2001;345:851 & 861)

- **Tailoring therapy**

  lifestyle Δs typically complementary rather than alternative to drug Rx [although if low risk (stage 1, no end-organ damage or risk factors), could start with lifestyle]

  if stage 1, start w/ monoRx; if stage 2, consider starting w/ combo (eg, ACEI + CCB; *NEJM* 2008;359:2417), as most will require ≥2 drugs

  typically start drug at ½ maximal dose; after 2-3 wk either titrate up or add new drug

Resistant hypertension (*JAMA* 2014;311:2216)

- BP > goal on ≥3 drugs incl diuretic, ~12-13% of hypertensive population (HTN 2011;57:1105)
- Differentiate between true & *pseudoresistance,* w/ latter due to: inaccurate measurement or use of wrong cuff size poor dietary compliance (Na/K intake, can assess w/ 24-hr urine for Na, K and Cr) suboptimal med dosing (eg, <50% of max dose) or poor med compliance volume expansion (inadequate diuretic dosing) white coat HTN (consider ABPM) 2° causes or external drivers (eg, OSA, steroids, NSAIDS, alcohol) (*Lancet* 2010;376:1903)
- True resistance = uncontrolled BP confirmed by ABPM despite compliance w/ optim. doses
- Treatment considerations:

  Persistent ↑ volume may contribute even if on standard HCTZ (*Archives* 2008;168:1159).

  Effective diuretic dosing required for most to achieve control (HTN 2002;39:982).

  Chlorthalidone over HCTZ (if renal function preserved). Loop diuretic favored over thiazide for initial Rx if eGFR <30; however, adding thiazide to loop can ↑ diuresis if insufficient response to loop alone.

  Adding aldosterone antagonist (if renal function preserved) (*PATHWAY-2, ESC* 2015)

  Adding β-blocker (particularly vasodilating ones such as labetalol, carvedilol, or nebivolol), centrally acting agent, α-blocker, or direct vasodilator

  Other Rx under investigation: renal denervation (see below); carotid baroreceptor stimulation; central AV anastomosis ↑ SBP by ~23 mmHg (*Lancet* 2015;385:1634)

- **Renal denervation:** catheter-based RF ablation of renal nerves modifying sympathetic outflow. Had appeared beneficial in unblinded and/or uncontrolled studies, but no effect on BP in controlled trial, so not currently an option in routine care (*NEJM* 2014;370:1393).

Special situations

- **Secondary causes**

  Renovascular (qv)

  Renal parenchymal disease: salt and fluid restriction, ± diuretics

  Endocrine etiologies: see "Adrenal Disorders"

- **Pregnancy:** methyldopa, labetalol, nifedipine, hydralazine; avoid diuretics; Ø ACEI/ARB

HYPERTENSIVE CRISES

- **Hypertensive emergency:** ↑ BP → acute target-organ ischemia and damage

  neurologic: encephalopathy (insidious onset of headache, nausea, vomiting, confusion), hemorrhagic or ischemic stroke, papilledema

  cardiac: ACS, HF/pulmonary edema, aortic dissection

  renal: proteinuria, hematuria, acute renal failure; scleroderma renal crisis

  microangiopathic hemolytic anemia; preeclampsia-eclampsia

- **Hypertensive urgency (severe asymptomatic HTN):** SBP >180 or DBP >120 (?110) w/ minimal or no target-organ damage

Precipitants

- Progression of essential HTN ± medical noncompliance (espec clonidine) or Δ in diet
- Progression of renovascular disease; acute glomerulonephritis; scleroderma; preeclampsia
- Endocrine: pheochromocytoma, Cushing's
- Sympathomimetics: cocaine, amphetamines, MAO inhibitors + foods rich in tyramine
- Cerebral injury: do *not* treat HTN in acute ischemic stroke unless Pt getting lysed, extreme BP (>220/120), Ao dissection, active ischemia or HF (*Stroke* 2003;34:1056)

Treatment (*Chest* 2007;131:1949)

- Tailor goals to clinical context (eg, more rapid lowering for Ao dissection)
- Emergency: ↓ MAP by ˜25% in mins *to 2* h w/ IV agents (may need arterial line for monitoring); goal DBP <110 w/in 2-6 h, as tolerated
- Urgency: ↓ BP to ≤160/100 in *hrs* using PO agents; goal normal BP in ˜1-2 d
- Watch UOP, Cr, mental status: may indicate a lower BP is not tolerated

Drugs for Hypertensive Crises

IV	Nitroprusside* 0.25-10 mcg/kg/min	Nitroglycerin 5-1000 mcg/min
	Labetalol 20-80 mg IVB q10min or 0.5-2 mg/min	Esmolol 0.5 mg/kg load → 0.05-0.2 mg/kg/min
	Fenoldopam 0.1-1.6 mcg/kg/min	Hydralazine 10-20 mg q20-30 min

	Nicardipine 5-15 mg/h	Clevidipine 1-16 mg/h
	Phentolamine 5-15 mg bolus q5-15min	Enalaprilat 1.25 mg
	Captopril 12.5-100 mg tid	Labetalol 200-800 mg tid
PO	Clonidine 0.2 mg load → 0.1 mg qh	Hydralazine 10-75 mg qid

*Metabolized to cyanide → Δ MS, lactic acidosis, death. Limit use of very high doses (8-10 mcg/kg/min) to <10 min. Monitor thiocyanate levels. Hydroxocobalamin or sodium thiosulfate infusion for treatment of cyanide toxicity.

Treatment Considerations for Specific Clinical Settings

Clinical	Setting Note	Treatment
Acute stroke	BP ↓ must be balanced w/ risk of worsening ischemia	Consult stroke team
Aortic dissection (qv)	✓ BP in both arms and treat higher value	βB first, then add vasodilator (eg, nitroprusside) if needed
Acute pulm edema	Avoid ⊖ inotropes (eg, βB) if LV dysfxn, unless ischemia	Vasodilator (eg, NTG) and loop diuretic
Antihypertensive withdrawal	Suspect if abrupt d/c of symp. blocker (eg, clonidine)	Restart d/c'd drug or consider labetalol or nitroprusside
Sympathetic activity (pheo, auton dysfxn, cocaine, MAO + tyramine-containing foods)	Avoid βB as could → unopposed α in vasculature → vasconstriction and further ↑ BP	Phentolamine (pheochromocytoma), nitroprusside

RENOVASCULAR DISEASE

Pathophysiology

- ↑ renal perfusion → activation of RAA system → vasoconstriction, ↑ aldo & vasopressin, ↑ sympathetic activity → volume retention & HTN → progressive renal dysfxn and CV risk

- Unilateral stenosis ↑ HTN
- Bilateral (or unilat involving solitary functioning kidney) → HTN & progressive renal insuffic

Etiologies

- **Atherosclerosis** (˜90%): usually involving ostial or prox segments. Often incidental finding as common in Pts w/ established athero (eg, CAD, PAD) but uncommon cause of HTN.
- **Fibromusclar dysplasia** (FMD, ˜10%): nonathero medial fibroplasia usually mid/distal female-predominant (85-90%); mean age 52 y (*Circ* 2012;125:3182) characteristic “string of beads” appearance (or concentric smooth stenosis) on angio usually > 1 territory involved (eg, carotid in ˜65%), explaining sx of HA, dizziness, tinnitus
- Other (uncommon): vasculitis (Takayasu's, GCA, PAN or eosinophilic granulomatosis w/ polyangiitis) often w/ ↑ inflammatory markers, systemic s/s; scleroderma; local aneurysm or dissection; embolism; retroperitoneal fibrosis

Diagnosis

- Consider testing if any of the following *and* if finding would modify treatment:

  Clinical picture consistent w/ secondary HTN w/ no other compelling etiology Severe HTN (SBP ≥180 and/or DBP ≥120 mmHg) and/or flash pulm edema/CHF Progressive renal insufficiency w/ bland sediment, unilateral small kidney (≤9 cm), renal asymmetry > 1.5 cm, or acute sustained Cr ↑ by ≥30% w/in 1 wk of starting ACEI/ARB

Testing for Renovascular Disease (*Am Fam Physician* 2009;80:273)

Modality	Se	Sp	Notes
Duplex Doppler US	85%	92%	Pt habitus & operator dependent. May be preferred if renal dysfxn. Allows quantification of resistive index.*
CTA	88-96%	97%	Less sensitive (˜30%) for distal disease such as FMD Contrast agent nephrotoxic
MRA	88-100%	>95%	Less sensitive (˜30%) for distal disease such as FMD Risk of nephrogenic systemic fibrosis if mod-sev CKD
Angiography (DSA)	gold standard		Allows measurement of gradients Invasive, contrast agent nephrotoxic
Plasma Renin Activity (PRA)	50-80%	low	Not 1st line. Can ↑ Se by measuring 1 hr after capto administration
Captopril Renal Scan	75-100%	n/a	Not 1st line, but can determine hemodynamic signif of stenosis. Not reliable in bilateral RAS or poor renal fxn.

*Resistive index = [(peak syst vel - end diast vel) / peak syst vel].

- Monitoring: for athero, repeat imaging only necessary if Δ in clinical status that would lead to intervention; for FMD image q6-12mo to assess for progression

Treatment

- If due to atherosclerosis, risk factor modification: quit smoking, ↓ chol
- Antihypertensive Rx effective for most Pts: diuretic + ACEI/ARB (watch for ↑ Cr) or CCB
- Revascularization (typically percutaneous w/ stenting):

  Had considered if refractory HTN, recurrent flash pulm edema, worsening CKD

  However, clinical trials enrolling stable Pts w/ mod stenosis (50-70%) and HTN on ≥2 agents showed no benefit on # of BP meds, renal fxn or CV outcomes (*NEJM* 2000;342:1007; 2009;361:1953; 2014;370:13). Unknown if beneficial in more severe stenoses or in higher-risk Pts (eg, recent CHF, >3 meds).

  Resistive index >80 on U/S implies intrinsic renal damage and thus less likely to benefit from revasc, so may predict outcome after intervention (*NEJM* 2001;344:410). Operator dependent and some studies have not replicated findings, so not utilized broadly.

  Renal vein renin measurements, PRA, captopril renogram may provide supportive evidence as to hemodynamic significance of RAS, but limited utility due to low Se

  For FMD (usually more distal lesions): PTA ± bailout stenting
- Surgery (very rare): resection of pressor kidney
- Bilateral RAS: 20-46% of Pts w/ RAS. Associated w/ higher creatinine and worse CV outcomes. In addition to anti-HTN Rx, consider revasc if likely to benefit (failure of meds, recurrent pulmonary edema, progressive renal failure). Trials including Pts w/ bilateral RAS did not show benefit but included moderate stenoses.

AORTIC ANEURYSMS

Definitions

- **True** aneurysm (≥50% dilation of all 3 layers of aorta; <50% called ectasia) vs **false or pseudoaneurysm** (rupture contained by adventitia)
- **Location:** root (annuloaortic ectasia), thoracic aortic aneurysm (TAA), thoracoabdominal aortic aneurysm (TAAA), abdominal aortic aneurysm (AAA)
- **Type:** fusiform (circumferential dilation) vs saccular (localized dilation of aortic wall)

Epidemiology (*Circ* 2010;121:e266, 2011;124:2020 & 2013;127:e6; *Nat Rev Cardiol* 2011;8:92)

- In U.S., ~15,000 deaths/y from aortic ruptures; overall ~50,000 deaths/y from Ao disease
- **TAA:** 10/100,000 Pt-yrs, ♂:♀ 2:1; ~60% root/ascending; 40% descending

- **AAA:** ~4-8% prev in those >60 y (although may be ↓ ; *Circ* 2011;124:1118); 4-6× more common in ♂ vs ♀; mostly infrarenal
- Arch & TAAA rarer

Pathophysiology (*NEJM* 2009;361:1114; *Nat Med* 2009;15:649)

- Medial degeneration and/or ↑ wall stress

  Medial degeneration = muscle apoptosis, elastin fiber weakening, mucoid infiltration

  Wall stress ∝ [(ΔP × r) / (wall thickness)], LaPlace's law
- **TAA:** most commonly medial degeneration; seen w/ connective tissue disorders & aortitis
- **AAA:** most commonly long-standing HTN + athero/inflammation → medial weakening

Risk factors

- Classic: **HTN**, **atherosclerosis**, **smoking**, **age**, **male sex**
- **Marfan syndrome** (mutations in fibrillin-1, *FBN*-1): cardinal features are Ao root aneurysm & ectopia lentis. Other suggestive signs include: tall stature; arachnodactyly w/ *thumb sign* (entire distal phalanx of adduct. thumb extends beyond ulnar border of palm) and/or *wrist sign* (tip of thumb covers 5th finger fingernail when wrapped around contralat wrist); pectus deformities; scoliosis; dural ectasia; spontaneous PTX; MVP.
- **Loeys-Dietz syndrome** (mutation in TGF-β receptors 1 or 2, *TGFBR1/2*): triad of arterial tortuosity & aneurysms, widely spaced eyes, bifid uvula or cleft palate. Also w/ velvety & hyperlucent skin and bluish sclera.
- Vascular **Ehlers-Danlos syndrome** (mutation in type III procollagen, *COL3A1*): easy bruising; thin, translucent skin w/ visible veins (but not excessively stretchable); acrogeria (aged appearance of hands & feet); flexible digits; uterine or intestinal rupture; distinctive facial features (protruding eyes, thin nose & lips, sunken cheeks, small chin)
- Other genetic disorders: **bicuspid AoV**; Turner syndrome (45X; short stature, ovarian failure, Ao coarctation); other familial aortopathies (mutations in smooth muscle myosin & actin genes including MYH11 and ACTA2)
- **Aortitis:** Takayasu's, GCA, spondyloarthritis, IgG4-related disease
- **Infection** (ie, mycotic aneurysm): salmonella, TB, syphilis

Screening (*Circ* 2010;121:e266 & 2011;124:2020; *Annals* 2014;161:281; *JAMA* 2015;313:1156)

- **TAA:** if bicuspid AoV or 1° relative w/: (a) TAA or bicuspid valve, (b) Marfan, Loeys-Dietz, Turner; known relevant genetic mutation (see above)
- **AAA:** ✓ for pulsatile abd mass; U/S ♂ >60 y w/ FHx of AAA & ♂ 65-75 y w/ prior tobacco

Diagnostic studies (*Circ* 2010;121:e266 & 2011;124:2020)

- **Contrast CT:** quick, noninvasive, high Se & Sp for all aortic aneurysms
- **TTE/TEE:** TTE most useful for root and proximal Ao; TEE can visualize other sites of TAA
- **MRI:** preferred over CT for aortic root imaging for TAA; also useful in AAA but time-consuming; noncontrast “black blood” MR to assess aortic wall

- **Abdominal U/S:** screening and surveillance test of choice for infrarenal AAA

Treatment principles (*Circ* 2006;113:e463; 2008;117:1883; 2010;121:1544 & e266)

- Goal is to prevent rupture (50% mortality prior to hospital) by modifying risk factors
- **Smoking cessation:** smoking associated w/ ↑ rate of expansion (*Circ* 2004;110:16)
- **Statin** (to achieve LDL-C <70 mg/dL): ↓ death and stroke & possibly ↓ rate of expansion (*Eur J Vasc Endovasc Surg* 2006;32:21)
- **BP control: βB** (↓ dP/dt) ↓ aneurysm growth (*NEJM* 1994;330:1335)

  ACEI a/w ↓ risk of rupture (*Lancet* 2006;368:659)

  ARB may ↓ rate of aortic root growth in Marfan (*NEJM* 2008;358:2787)

  βB and ARB similar ↓ rate of Ao root growth in children and young adults w/ Marfan (*NEJM* 2014;371:2061)

- Moderate cardiovascular exercise okay, but no burst activity/exercise requiring Valsalva maneuvers (eg, heavy lifting)
- **Indications for intervention** (surgery/endovascular repair)

  Individualize based on FHx, body size, gender, anatomy, surgical risk

  TAA (*Circ* 2010;121:1544 & e266) symptoms

  ascending Ao ≥5.5 cm (4-5 cm if Marfan, bicuspid AoV, Loeys-Dietz, vascular EDS, or other genetic/familial disorder)

  descending >6 cm ↑ >0.5 cm/y

  aneurysm >4.5 cm and planned AoV surgery

  AAA (*NEJM* 2002;346:1437 & 2014;371:2101) symptoms infrarenal ≥5.5 cm, but consider ≥5.0 cm in ♀ ↑ >0.5 cm/y; inflam/infxn

Surgery (*Circ* 2010;121:e266; *EHJ* 2014;25:2873)

- Ascending aorta

  No root involvement: resection & replacement w/ Dacron tube graft

  Root involvement: need to address AoV integrity; depending on AoV itself: modified Bentall: Dacron Ao root + prosthetic AoV, reattach coronaries valve-sparing: reimplant native AoV in Dacron Ao graft; reattach coronaries

- Arch: high-risk, complex surgery because of the arch branches; variety of combinations of partial/complete resection, stent graft & bypass of arch vessels
- Descending thoracic aorta: resection & grafting vs endovascular repair (qv)

Endovascular repair (EVAR) (*NEJM* 2008;358:494; *Circ* 2011;124:2020 & 2015;131:1291)

- Depends on favorable aortic anatomy
- TEVAR (thoracic EVAR) for descending TAA ≥5.5 cm may ↑ periop morbidity and possibly mortality (*Circ* 2010;121:2780; *JACC* 2010;55:986; *J Thorac CV Surg* 2010;140:1001 & 2012;144:604)
- AAA

Guidelines support open repair or EVAR for infrarenal AAA in good surg candidates ↓ short-term mort., bleeding, LOS; but long-term graft complic. (3-4%/y; endoleak, need for reintervention, rupture) necessitate periodic surveillance, with no proven Δ in overall mortality in trials, except ? in those <70 y (*NEJM* 2010;362:1863, 1881 & 2012;367:1988)

In observational data, EVAR assoc w/ ↑ survival over 1st 3 y, after which survival similar. Rates of rupture over 8 y 5.4% w/ EVAR vs 1.4% w/ surgery (*NEJM* 2015;373:328)

In Pts unfit for surgery or high periop risks: ↓ aneurysm-related mortality but no Δ in overall mortality over medical Rx (*NEJM* 2010;362:1872). EVAR noninferior (? superior) to open repair in ruptured AAA w/ favorable anatomy (*Ann Surg* 2009;250:818).

- Pt selection for endovascular includes requirement to comply with long-term surveillance

Complications (*Circ* 2010;121:e266; *Nat Rev Cardiol* 2011;8:92)

- **Pain:** gnawing chest, back or abdominal pain; new or worse pain may signal rupture
- **Rupture:** risk ↑ w/ diameter, ♀, current smoking, HTN

  TAA: ~2.5%/y if <6 cm vs 7%/y if >6 cm

  AAA: ~1%/y if <5 cm vs 6.5%/y if 5-5.9 cm rupture p/w severe constant pain and hemorrhagic shock; ~80% mortality at 24 h
- **Aortic insufficiency (TAA)** and **CHF**
- **Acute aortic syndromes** (qv)
- **Thromboembolic ischemic events** (eg, to CNS, viscera, extremities)
- **Compression of adjacent structures** (eg, SVC, trachea, esophagus, laryngeal nerve)

Follow-up (*Circ* 2010;121:1544 & e266; *Nat Rev Cardiol* 2011;8:92; *JAMA* 2013;309:806)

- Expansion rate ~0.1 cm/y for TAA, ~0.3-0.4 cm/y for AAA
- AAA: <4 cm q2-3 yrs; 4-5.4 cm q6-12 mos; more frequent if rate of expansion >0.5 cm in 6 mo
- TAA: 6 mo after dx to ensure stable, and if stable, then annually (*Circ* 2005;111:816)
- Screen for CAD, PAD and aneurysms elsewhere, espec popliteal. About 25% of Pts w/ TAA will also have AAA, and 25% of AAA Pts will have a TAA: consider pan-Ao imaging.
- Patients with endovascular repair require long-term surveillance for endoleak & to document stability of aneurysm

ACUTE AORTIC SYNDROMES

Definitions (*Circ* 2005,112:3802 & 2010;121:e266; *Eur Heart J* 2012;33:26)

- **Aortic dissection** (AoD): intimal tear → blood extravasates into Ao media (creates false lumen). Rate 3-16/100,000 Pt-yrs. False lumen acts as "wind sock," ↑ in size and compressing true lumen (patency of false lumen associated with outcome).
- **Intramural hematoma** (IMH): vasa vasorum rupture → medial hemorrhage that does not communicate with aortic lumen; 6% of aortic syndromes; clinically managed as AoD

- **Penetrating ulcer** (PAU): atherosclerotic plaque penetrates elastic lamina → medial hemorrhage. PAU in setting of IMH assoc. w/ similar outcomes as AoD. Outcomes for isolated PAU less well defined but considered AAS. Rx depends on clinical context.

Classification (proximal twice as common as distal)

- **Proximal:** involves ascending Ao, regardless of origin (= Stanford A, DeBakey I & II)
- **Distal:** involves descending Ao only, distal to L subclavian art. (= Stanford B, DeBakey III)
- **Other Considerations:** isolated to arch generally treated as proximal; distal with involvement of subclavian depends on overall clinical picture.

Risk factors

- **Classic** (in older Pts): **hypertension** (h/o HTN in >70% of dissections); **age** (60s-70s), **male sex** (~70% ♂); **smoking**
- **Genetic or acquired predisposition** (may present younger; see "Aortic Aneurysms"):

  Connective tissue disease/congenital anomaly: Marfan, Loeys-Dietz, vascular Ehlers-Danlos, bicuspid AoV, coarctation (eg, in Turner's), other familial aortopathies, PCKD

  Aortitis: Takayasu's, GCA, Behçet's, syphilis

  Pregnancy: typically 3rd trimester
- Other environmental factors:

  Trauma: blunt, deceleration injury

  Cardiovascular procedures: IABP, cardiac or aortic surgery, cardiac catheterization

  Acute ↑ BP: cocaine, Valsalva (eg, weightlifting)

Clinical Manifestations and Physical Exam* (*JAMA* 2000;283:897)

Feature	Proximal	Distal
"Aortic" pain (abrupt, severe, tearing or ripping quality, *maximal at onset* [vs crescendo for ACS])	**94%** (chest, back)	**98%** (back, chest, abd)
Syncope (often due to tamponade)	**13%**	4%
HF (usually due to acute AI)	**9%**	3%
CVA	**6%**	2%
HTN	36%	**70%**
HoTN or shock (tamponade, AI, MI, rupture)	**25%**	4%

Pulse deficit (if involves carotid, subclavian, fem)	**19%**	**9%**
AI murmur	**44%**	12%

*S/S correlate w/ affected branch vessels & distal organs; may Δ as dissection progresses.

Initial evaluation (*Circ* 2010;121:e266)

- H&P, including bilateral BP and radial pulses for symmetry

  High-risk conditions: Marfan, CTD, FHx AoD, recent Ao manip., AoV dis., Ao aneurysm

  High-risk pain features: chest, back or abd pain described as [both (abrupt onset or severe intensity) and (ripping, tearing, sharp or stabbing) (absence ⊖ LR 0.3)]

  High-risk exam features:

  perfusion deficit [pulse deficit (⊕ LR 5.7), systolic BP differential (>20 mmHg), or focal neuro deficit + pain (⊕ LR >6)], or

  murmur of AI (new or not known to be old and in conjunction w/ pain), or hypotension or shock
- 12-lead ECG: often abnl but non-dx; may show STE if prox AoD involving coronary
- CXR: abnl in 60-90% [↑ mediast. (absence ⊖ LR 0.3), L pl effusion] but *cannot* r/o AoD
- *Obtain expedited Ao imaging if:* ≥2 high-risk features, 1 high-risk feature w/o clear alternative dx, or 0 features but unexplained HoTN or widened mediastinum on CXR

Diagnostic studies (*Circ* 2010;121:e266; *JACC CV Img* 2014;7:406)

- **CT:** quick, noninvasive, readily available, Se ≥93% & Sp 98%; however, if ⊖ & high clin. suspicion → additional studies (⅔ w/ AoD have ≥2 studies; *AJC* 2002;89:1235)
- **MRI:** Se & Sp >98%, but time-consuming test & not readily available
- Axial studies (CT, MRI) should be gated to ECG to evaluate Ao root; if high index of suspicion, study should include entire aorta (chest, abd, & pelvis)

- Echo

  TTE: low Se (∴ not dx study) but can show effusion, AI, & dissection flap (if proximal)

  TEE: Se >95% prox, 80% for distal; can assess cors/peric/AI; "blind spot" behind trachea
- **Aortography:** Se ~90%, time-consuming, cannot detect IMH; can assess branch vessels
- **D-dimer:** Se/NPV ~97%; ? <500 ng/mL to r/o dissec (*Circ* 2009;119:2702) but not in Pts at high clinical risk (doi:10.1016/j.annemergmed.2015.02.013); does not r/o IMH

Initial medical treatment (*Lancet* 2008;372:55; *Circ* 2010;121:1544; *JACC* 2013;61:1661)

- ↓ **dP/dt** targeting HR <60 & central BP <120 (or lowest that preserves perfusion; r/o pseudohypotension, eg, arm BP ↑ due to subclavian dissection; use highest BP reading)

- ***First* with IV βB** (eg, esmolol, labetalol) to blunt reflex ↑ HR & inotropy that would occur in response to vasodilators; verap/dilt if βB contraindic.
- ***Then* ↓ SBP with IV vasodilators** (eg, nitroprusside)
- HTN control may require multiple agents (median of 4 in one study; *J Hum Hypertens* 2005;19:227). If unable to control readily: 1st evaluate for complication (eg, visceral ischemia); Rx pain w/ MSO_4; if no complication, then consider other drivers (eg, EtOH withdrawal).
- **If HoTN:** urgent surgical consultation, IVF to achieve euvolemia, pressors to keep MAP 70 mmHg; r/o complication (eg, tamponade, contained rupture, severe AI)

Treatment of proximal AoD (*Circ* 2010;121:1544; *Lancet* 2015;385:800)

- *Acute:* all cases should be considered for emergent surgery

  root replacement; valve sparing unless bicuspid or valve involvement

  acute stroke should not necessarily dissuade from surgery (mortality w/o surgery ~100%, *Circ* 2013;128:S175)

  prior AoV surgery postulated to be protective from complications, but most would operate

  need for preop coronary angio debatable as procedure nontrivial in setting of dissection and likelihood of performing concomitant CABG low
- *Chronic:* consider surgery if complicated by progression, AI or aneurysm

Treatment of distal AoD (*Circ* 2010;121:1544; *JACC* 2013;61:1661; *Lancet* 2015;385:800)

- Intervention warranted if complication (see below)
- Endovascular intervention (fenestrate flap to decompress false lumen, open occluded branch, stent entry tear) may be preferred over surgery due to possible ↑ mort. (*JACC* 2013;61:1661 & *Circ* 2015;131:1291)
- Stent graft for *uncomplicated* cases may ↓ risk of aorta-related complications and adverse remodeling (*Circ Cardiovasc Interven* 2013;6:407)

Complications (occur in ~20%; *Circ* 2003;108:II-312 & 2010;121:e266)

- *Monitor all Pts w/ frequent assessment (sx, BP, UOP), pulse exam, labs (Cr, Hb, lactic acid), imaging (~7 d or sooner if sx or significant lab Δ)*
- *Uncontrolled BP despite intensive IV Rx or continued or → pain may indicate complication*
- **Progression:** propagation of dissection, ↑ aneurysm size, ↑ false lumen size
- **Rupture:** pericardial sac → tamponade (avoid pericardiocentesis unless PEA); blood in pleural space, mediast., retroperitoneum; ↑ in hematoma on imaging portends rupture
- **Malperfusion** (partial or complete obstruction of branch artery) can be *static* (avulsed/thrombosed) or *dynamic* (Δs in pressure in true vs false lumen) coronary → MI (usually RCA → IMI, since dissection often along outer Ao curvature) innominate/carotid → CVA, Horner intercostal/lumbar → spinal cord ischemia/paraplegia innominate/subclavian → upper extremity ischemia; iliac → lower extremity ischemia celiac/mesenteric → bowel ischemia (can be subtle w/ nonspecific GI sx, anorexia, pain) renal → acute renal failure or gradually ↑ Cr, refractory HTN
- **AI:** due to annular dilatation or disruption or displacement of leaflet by false lumen
- Mortality (*Circ* 2013;127:2031; *JACC* 2015;66:350)

~50% prior to hospital

historically ~1%/h × 48 h for acute prox AoD who survive to hospital w/ 47% subseq mort at 30 d; more recent data w/ 22% in-hospital mortality

13% at 30 d for acute distal overall but 25% if complications mortality similar for proximal and distal that survive to discharge: ~85% at 5 y

Long-term monitoring

- Major concern is progression to aneurysm or recurrent dissection
- Treat BP, risk factors aggressively
- **Serial imaging for all** (CT or MRI, latter may be preferred to lower cumulative radiation exposure) at 1, 3, and 6 mo, and then annually (18 mo, 30 mo, etc.)
- Pts treated endovascularly need close follow-up to monitor for complication (eg, endoleak)
- Partial thrombosis of false lumen associated with worse outcomes/mortality (*NEJM* 2007;357:349)
- In patients who present at young age or other indications of predisposing factor, consider genetic evaluation and screening of family members

PERIPHERAL ARTERY DISEASE (PAD)

Epidemiology and risk Factors

- Prev. ↑ w/ age: <1% if <40 y, ~15% if ≥70 y; risk factors incl. **smoking**, **DM**, HTN, chol
- More frequent in Pts w/ other symptomatic atherosclerotic disease (eg, coronary, carotid)
- Associated w/ ↑ risk of CV events (*JAMA* 2007;297:1197)
- If sx, 3-y risk of stroke ~3%, acute limb ischemia ~4%, periph revasc ~22% (*Circ* 2013;112:679)

Clinical Features

- **Asymptomatic** (~35%) or **atypical** sx (~40%): often undertreated in terms of risk factor modifying therapy (*Circ* 2011;124;17)
- **Claudication** (~25%): dull ache, often in calves precip by walking & relieved by stopping (vs spinal stenosis, qv)

  Leriche syndrome (aortoiliac occlusive disease): buttock & thigh claudication, ↑ or ø femoral pulses, & erectile dysfxn
- **Critical limb ischemia** (CLI, 1-2%): 1 or more of the following 3 manifestations

  rest pain: ↑ w/ elevation b/c ↓ perfusion

  ulcer: typically at pressure foci, often dry (in contrast, venous ulcers are more often at medial malleolus, wet, and with hemosiderin deposition)

  gangrene: more typically “dry” (ie, distal limb, dry shrunken and dark red, lack of pus) as a manifestation of ischemia due to impaired blood flow rather than “wet” (ie, infected, pus present, fetid smell), which may occur in the setting of infection or injury may be chronic (ie, sx >2-wk duration) vs acute limb ischemia, which is a

vascular emergency (see below)

a/w poor outcome: 45% amputation & 20% mortality at 6 mo (*J Vasc Surg* 2000;31:S1)

- Blue toe syndrome: most likely atheroembolic disease with occlusion of digital arteries

PAD Clinical Symptom Classification

Rutherford		Fontaine		Typical ABI*
Stage	**Definition**	**Stage**	**Definition**	
0	Asx	1	Asx	0.9-1.0
1	Mild claudication	2a	Sx at distance >650 ft	0.4-0.9
2	Mod claudication			
3	Severe claudication	2b	Sx at distance <650 ft	
4	Rest pain	3	Nocturnal or rest pain	<0.4
5	Ischemic ulceration not exceeding ulcer on digits of foot	4	Necrosis (death of tissue) and/or gangrene of limb	
6	Severe ischemic ulcers or frank gangrene			

*ABI is generally, but not absolutely correlated w/ clinical measures of lower extremity fxn & sx

Diagnosis

- Ddx includes

  nonvascular:

  neurogenic claudication (spinal stenosis): pain w/ standing, relieved by sitting, lying, or forward flexion; a/w neurologic abnl (weakness, sensory Δs, h/o deg. disc disease)

  musculoskeletal/arthritis: joint pain, morning stiffness, associated joint pathology or instability, crepitus or effusion

  Baker's cyst: posterior knee pain, knee stiffness, mass behind knee, discomfort w/ prolonged standing, impairment of bending

  non-athero vascular:

  venous claudication (uncommon): pain w/ walking in setting of proximal venous obstruction & no arterial obstruction

  dissection, embolism, aneurysm, or vasculitis

popliteal artery entrapment (exercise-induced lower leg pain)

- Physical exam: ↓ peripheral pulses ± femoral bruits if severe: pallor of feet w/ elevation, dependent rubor, cyanosis other signs of chronic PAD: hair loss/shiny or cool skin, skin atrophy, nail hypertrophy

Testing

- **Ankle:brachial index (ABI):** nl 1-1.4; borderline 0.91-0.99; abnl ≤0.90; if > 1.4, non-dx, likely due to calcified/noncompressible vessel
- **Toe:brachial index (TBI)** helpful if noncompressible (toe artery less likely to calcify); but ranges different than ABI (>0.7 nml, 0.5-0.7 mild, 0.35-0.5 mod, <0.35 mod-severe, severe if toe pressure <30 mmHg)

- **Segmental pressures** to determine level of disease (20 mmHg gradient between segments indicates stenosis)
- **Pulse volume recording (PVR)** done w/ segmental pressures: determine site and severity of disease. Abnormal waveform can indicate disease in noncompressible vessel, but pressures used over waveform if vessels are compressible.
- If ⊕ sx but nl ABI: ✓ **exercise ABI** (some consider even in asx Pt w/ risk factors for PAD if will modify therapy)
- Treadmill study (or 6-min walk test) to quantify magnitude of functional limitation
- **Imaging** (Duplex arterial U/S; CTA w/ distal run-off; MRA or angio) if dx in question or considering intervention. Some do routine Duplex U/S to monitor graft/stent patency.

Medical treatment (*JACC* 2013;61:1555; *JAMA* 2013;309:453; *Circ Res* 2015;116:1579)

- **Treat risk factors:** smoking cessation, high-intensity statin, control HTN & DM, smoking cessation (*JACC* 2010;56:2105). βB OK if indicated for another reason (eg, CAD, AF).
- **Antiplatelet Rx:** benefit shown primarily for ↑ CV risk (*BMJ* 2002;324;71)

  If asx: benefit of antiplt Rx unclear espec if ABI only borderline (*JAMA* 2010;303;9)

  If sx: ASA or clopidogrel

  ASA: 23% ↓ risk of major CV events seen in meta-analysis of older studies (mostly ASA but also other antiplatelet Rx) (*BMJ* 2002;324:71)

  Clopidogrel: superior to ASA, but single, older study (*Lancet* 1996;348:1333)

  ASA+clopi may be better than ASA alone, but only posthoc data (*EHJ* 2009;30:1992)

  Vorapaxar (PAR-1 antag.) further ↓ risk on top of ASA or clopidogrel (*Circ* 2013;112:679)
- Anticoagulation w/ warfarin not beneficial (*NEJM* 2007;357:217)
- **ACEI/ARB** to ↓ CV risk (*NEJM* 2000;342:145)
- **Improve claudication**

  Supervised exercise: sx-limited, ≥3×/wk, ≥30-45 min/session, ↑ as tolerated; beneficial including ↑ walking time 50-200% (*Cochrane* 2014;7:CD990); structured exercise more effective than home-based, but home-based still effective (*JAMA* 2013;310:57)

  ACEI & statins may ↓ sx (*Circ* 2003;108:1481)

  Cilostazol (nb, interacts w/ diltiazem & omeprazole; may cause headache or diarrhea; do not use in Pts w/

CHF); pentoxifylline likely less effective

- **Limb preservation:** foot exams for ulcers/wounds, revasc (qv), vorapaxar (PAR-1 antag) ↓ acute limb ischemia (*Circ* 2013;112:679), statin use assoc. w/ ↓ amput (*EHJ* 2014;35:2864)

Revascularization

- Consider if limiting sx despite exercise/medical Rx or if CLI; also consider as 1st-line Rx for isolated aortoiliac disease given high rate of long-term patency (*Circ* 2013;128:2704)
- **Endovascular** (angioplasty or stenting) usually favored over **surgical** (bypass or endarterectomy), but depends on lesion complexity & location (aortoiliac or "inflow" vs infrainguinal or "outflow") and Pt comorbidities
- Decision for stent vs angioplasty alone depends on lesion length & complexity, location (eg, over joints) (*J Vasc Surg* 2007;33:S1)
- Angioplasty w/ paclitaxel-coated balloon associated with ↑ primary patency vs regular balloon for femoropopliteal disease (*NEJM* 2015;373:145)
- Durability of endovascular revascularization depends in part on location, with greater longterm patency for iliac vs femoral interventions (*JACC* 2006;47:e1)
- Dual antiplatelet (DAPT, ASA + clopidogrel) commonly prescribed after endovascular intervention for 1-3 mo, but no prospective data. DAPT after bypass surgery not beneficial overall but possibly in subgroup w/ prosthetic grafts (*J Vasc Surg* 2010;52:825).
- Anticoagulation with warfarin does not improve patency (*NEJM* 2007;357:217), but may be indicated in subgroups with high thrombotic risk
- Stents not ferromagnetic, so MRI safe, but both MRI & CT may have artifact. Duplex U/S useful to assess stent patency and is used by some for serial routine monitoring of stent or graft patency, even in asx Pts.
- If coronary angiography needed, avoid access through CFA stent or femoral bypass

Acute limb ischemia (ALI)

- Sudden decrement in limb perfusion that threatens viability; *viable* (no immed threat of tissue loss): audible art. Doppler signals, sensory & motor OK *threatened* (salvage requires prompt Rx): loss of arterial Doppler signal, sensory or motor
- Etiologies: embolism > acute thrombosis (eg, athero, APLA, HITT), trauma to artery
- Clinical manifestations (**6 Ps**): pain (distal to proximal, ↑ in severity), poikilothermia, pallor, pulselessness, paresthesias, paralysis
- Testing: thorough pulse & neuro exam; arterial Doppler; angiography, either CT w/ bilateral run-off through feet or arteriography
- Urgent consultation w/ vascular medicine and/or vascular surgery
- Treatment: immediate anticoagulation ± intra-arterial lytic; angioplasty or surgery

CEREBROVASCULAR DISEASE

EXTRACRANIAL DISEASE

Pathobiology

- Involving portions of carotid or vertebral arteries outside skull. Most commonly at carotid bifurcation but may involve common (CCA), internal (ICA), or external carotid (ECA).
- Most common etiology is athero; others include FMD, vasculitis, dissection, & radiation
- Associated w/ ↑ risk of systemic CV events including ipsilateral TIA/stroke
- Progressive narrowing, thrombosis or unstable plaque in CCA or ICA → embolization and/or ↑ distal perfusion → ischemia → TIA/stroke
- Asx *chronically occluded* vessel associated w/ low risk, as no embolization and Circle of Willis provides collateral flow

Diagnosis (*Circ* 2011;124:354)

- Stenosis defined as % lumen diameter at most severe stenosis relative to either ICA, probable lumen diameter at site of stenosis, or proximal common carotid (*J Neuroimaging* 1994;4:222). Significant stenosis is >50%.
- Carotid bruit suggestive but not sensitive
- **Duplex U/S:** Se >80%, Sp ~85%; 1st-line test

  Peak systolic velocity (PSV) for severity

  ↑ end diastolic velocity (EDV), spectral broadening, carotid index (ratio of PSV in ICA vs CCA) and echolucent plaque each associated w/ ↑ risk

  PSV >200 cm/s + EDV > 140 cm/s + carotid index > 4.5 has Se 96% for significant stenosis (*Stroke* 1996;27:1965; *Mayo Clin Proc* 2000;75:1133)
- Transcranial Doppler (TCD) as adjunct to U/S may show severe stenosis, evidence of occlusion (collateral flow), or microemboli by high-intensity signal transients (HITS)
- If significant but nonsevere stenosis, repeat study at 6 mo to determine if stable and then annually thereafter
- If stenosis appears severe (≥70%) or requires further characterization, then either CT angio (Se ~90%, Sp ≥95%) or MRA (Se ~95%, Sp ≥95%). Caution with contrast & risk of either renal dysfxn (CTA) or nephrogenic systemic fibrosis (MRA).
- Angiography gold standard but invasive and assoc w/ risk of stroke

Asx carotid stenosis (*Curr Treat Opt CV Med* 2013;252:63; *Expert Rev CV Ther* 2014;12:437)

- Cause of <15% of strokes and risk <1% annually in Pts on standard med Rx (see below)
- General management

  lifestyle intervention (smoking cessation, diet modification, exercise)

  antiplatelet therapy: ASA 75-325 mg/d or clopidogrel 75 mg/d if ASA allergic (*Circ* 2011;124:354)

  high-intensity statin (see "Lipids") and **BP control** (see "HTN")
- **Revascularization** (see options below) for selected Pts w/ ≥70% stenosis

  older trials have shown ↓ stroke risk vs med Rx alone, but not compared to modern med Rx (*NEJM*

1993;328:221; *JAMA* 1995;273:1421; *Lancet* 2004;363:1491)

due to low rate of associated stroke, absolute risk reduction likely small and benefit of intervention debated

consider Pt preference, risk of procedure, overall life expectancy (eg, ≥5 y), gender (benefit less certain in women), lesion characteristics of ↑ stroke risk (eg, echolucent plaque, TCD evidence of microemboli)

Symptomatic carotid stenosis (*NEJM* 2013;369:12)

- Symptomatic stenosis indicative of severe/unstable plaque and associated w/ ↑ risk of stroke. ∴ determination of sx important regarding treatment plan.
- Defined as recent (<6 mo) focal neurologic sx, sudden in onset, referable to carotid distribution. May include TIA or minor stroke [incl amaurosis fugax (transient monocular blindness)]. Vertigo & syncope unlikely related and generally not considered sx.
- For acute treatment for stroke, see “Stroke”
- All Pts w/ sx stenosis should receive med Rx as above
- Revascularization (*NEJM* 1991;325:445; *Lancet* 2004;363:915)

  recommended for 70-99% stenosis, generally w/in 2 wk unless severe comorbidity w/ limited lifespan, severe ipsilateral stroke w/ persistent deficit, occluded carotid, or high operative risk (≥6%)

  consider for 50-69% stenosis, depending on Pt-specific factors

  not indicated if <50% stenosis

Revascularization options

- **Carotid endarterectomy** (CEA): gold standard. Risk of procedural stroke or death <3% for asymptomatic disease and <6% for sx disease in experienced centers.
- Carotid artery stenting (CAS; *JACC* 2014;64:722): compared w/ CEA, periprocedural risk of stroke ↑ (espec in elderly) & MI ↑ (although many asx), subsequent rates of stroke similar (*NEJM* 2010;363:11; *Lancet* 2010;376:1062). Consider if not surgical candidate (anatomy or comorbidities). Generally requires DAPT (ASA + clopidogrel) for 30 d.

INTRACRANIAL DISEASE

- Cerebral and basilar arteries and distal branches thereof
- Most common etiology is athero & assoc w/ traditional athero risk factors (*Circ* 2014;1407:14); others include: dissection, FMD, vasoconstriction, vasculitis, moyamoya
- Estimated to cause 5-10% of ischemic strokes and more prevalent among blacks, Hispanics and Asians (*Stroke* 1995;26:14)
- Diagnosis: MRA, CTA, or TCD vs angio (see above); duplex U/S not useful
- Medical treatment similar as in extracranial; however, consider ASA+clopidogrel for sx disease for 90 d (*NEJM* 2011;365:993)
- Stenting and intracranial bypass not shown to be beneficial and not routinely recommended (*NEJM* 2011;365:993; *JAMA* 2015;313:1240)

PHARMACOLOGIC SECONDARY STROKE PREVENTION

Antiplatelet therapy (*NEJM* 2012;366:1914)

- In general monotherapy preferred to multiagent therapy for long-term prevention due to ↑ ICH risk w/ multiagent therapy
- **ASA:** ↓ death & repeat stroke; equal to warfarin in nonembolic stroke (*NEJM* 2001;345:1444)
- **Clopidogrel:** marginally superior to ASA, slightly ↑ ICH (*Lancet* 1996:348:1329)
- **Multiagent antiplatelet therapy:**

  ASA + clopi: not more effective than ASA alone and ↑ bleeding & ICH (*Lancet* 2004;364:331; *NEJM* 2012;367:817). In *minor stroke/*TIA, ASA + clopi × 21 d → clopi monoRx vs ASA monoRx resulted in ↓ stroke w/o ↑ ICH (*NEJM* 2013;369:11).

  ASA + dipyrimadole: superior to ASA (*Lancet* 2006;367:1665), but ↑ ICH and poor compliance

  Addition of vorapaxar to ASA or ASA+clopi ↑ first stroke in Pts w/ athero, but contra-indicated in patients w/ prior stroke due to ICH risk (*NEJM* 2012;366:1404; *Stroke* 2013;691:8)

Anticoagulation

- Not routinely indicated. Anticoag if cardiac/paradoxical emboli (except bacterial endocarditis) or hypercoag state. See "AF" and "VTE" for details.
- **Hold off on anticoag** in large strokes for ~2-4 wk given risk of hemorrhagic conversion.

Risk factor management

- BP (see "HTN"): long-term SBP target 120-139 mmHg (*JAMA* 2011;306:2137)
- LDL: high-intensity statin therapy (*Circ* 2014;129(*Suppl* 2):S1)

OTHER CEREBROVASCULAR DISEASES

Cervical artery dissection

- May involve intracranial or extracranial arteries. Manifests as luminal stenosis, thrombo-embolism or aneurysm. ~20% of ischemic strokes in young Pts (primarily embolic).
- Etiologies: trauma, physical activity, ? neck manip.; can be spontaneous (if assoc cond.)
- FMD most common assoc. condition (seen in 15-20%). Others infrequent: vascular EDS, Marfan, osteogenesis imperfect, homocystinuria, PKD, α_1-AT.
- Most (>60%) report HA or neck pain, Horner's in ~25%, tinnitus, rarely eye pain
- Imaging may show "crescent sign" of hematoma, string sign, tapering stenosis, flap or dissected aneurysm. Duplex U/S can be initial screen but lower Se (68-95%) and limited utility at skull base. CTA & MRA w/ similar Se & Sp; angio if inconclusive noninvasive imaging.
- Treatment: if stroke, see "Stroke." In general, thrombolysis should not be withheld if indicated. If SAH, manage accordingly.
- Antithrombotic therapy: either anticoagulation (AC) or antiplatelet Rx may be considered for extracranial dissection; however, large meta-analysis showed no benefit of AC over antiplatelet

  Rx (*Neurology* 2012;79:686). If AC chosen, typically for 3-6 mo, then Δ to antiplatelet. Intracranial dissection treated with antiplatelet monotherapy and not AC.

- Endovascular therapy or surgery considered for selected Pts, particularly if recurrent ischemia; however, no trials to demonstrate benefit.

Patent foramen ovale (PFO; in ˜27% of population) (*NEJM* 2005;353:2361)

- ↑ stroke risk: ≥4-mm separation, R → L shunting at rest, ↑ septal mobility, atrial septal aneurysm
- If PFO & stroke/TIA: no benefit of warfarin over ASA (*Circ* 2002;105:2625), but consider if at high risk for or has DVT/PE. No sig benefit shown for PFO closure so far, albeit studies small & w/ favorable trends (*NEJM* 2012;366:991; 2013:1083 & 1092).

Intracranial aneurysm (*Stroke* 2015;46:2368)

- Prevalence of saccular aneurysms 3.2%, w/ equal sex ratio (*Lancet Neurol* 2011;10:626); 20-30% having > 1 aneurysm
- Associated with family hx, hereditary syndromes (eg, EDS, polycystic kidney), smoking, HTN, aortic coarctation, ? estrogen deficiency (female preponderance after menopause) (*Stroke* 2001;32:606)
- Clinical presentations: most commonly incidental finding on brain imaging may be found in those presenting with SAH, which typically presents as “worst headache of my life,” ± syncope, nausea, vomiting, meningismus (*Neurology* 1986;36:1445) rarely unruptured aneurysms become symptomatic (eg, headache, visual change, cranial neuropathy, facial pain)
- Diagnosis: CTA or MRA
- Instruct Pt to avoid smoking, heavy EtOH use, illicit drugs, straining/Valsalva
- Treatment requires consideration of size, location, Pt age and comorbidities. In general: if sx or SAH → repair if no sx/SAH and ≥7-10 mm, consider repair if <7 mm observe (CTA or MRA q6mo and every 2-3 y once showing no Δ) endovascular coiling ↑ periprocedural morbidity & mortality vs surgical clipping, but ↑ risk of recurrence

Extracranial aneurysm

- Rare (<1% of arterial aneurysms) (*Surgery* 1983;93:319)
- True aneurysm may be associated with athero, trauma, dissection (qv), infection, vasculitis or radiation. Male:female predominance (2:1).
- Infected pseudoaneurysm may occur at site of prior carotid intervention.
- Clinical presentation: TIA/stroke; less likely mass effect or rupture
- Diagnosis: see approach for carotid disease above
- Instruct Pt to avoid smoking, heavy EtOH use, illicit drugs, straining/Valsalva
- Treatment: sx disease should be repaired; consider repair if asx and >2 cm, w/ thrombus, or ≤2 cm but ↑ 'ing. Surgical and endovascular options depending on anatomy & Pt risk.

Cerebral venous thrombosis (CVT) (*Circ* 2012;125:1709)

- Uncommon (<2/100,000/yr); female predominance (3× more common)
- >85% w/ risk factor including: hypercoagulable state, OCP, pregnancy, malignancy, infection, prior trauma, vasculitis, other inflammatory states (eg, IBD), hematologic disorders, nephrotic syndrome

- Clinical presentation variable and includes HA (˜90%), seizure, focal deficits, encephalopathy, sx of isolated intracranial hypertension (HA ± vomiting, papilledema, visual problems) may occur if hemorrhage or edema
- Diagnose w/ MR venography or CT venography (traditional head CT normal in ˜30% of CVT). D-dimer may be elevated but does not reliably exclude.
- Acute treatment

  treat elevated ICP

  consider antiseizure Rx if seizure on presentation or otherwise high risk

  anticoagulation (UFH or LMWH; see VTE for dosing) if no contraindication (nb, presence of ICH not absolute contraindication)

  consider endovascular venous recanalization with direct thrombolysis if progressive neurologic worsening despite anticoagulation
- Chronic treatment

  anticoagulation w/ VKA w/ INR 2-3 for 3-6 mo if provoked or 6-12 if unprovoked

  consider indefinite duration if recurrent, complicated by DVT or PE, or severe thrombophilia

  if occurred in setting of OCP, change to nonestrogen-based contraception
- Monitoring: imaging at 3-6 mo after dx to assess for recanalization

VENOUS THROMBOEMBOLISM (VTE)

Definitions

- Superficial thrombophlebitis: pain, tenderness, erythema along superficial vein
- Deep venous thrombosis (DVT)

  Proximal: thrombosis of iliac, femoral, or popliteal veins (nb, “superficial” femoral vein part of deep venous system)

  Distal: calf veins below knee; lower risk of PE/death than prox (*Thromb Haem* 2009;102:493)
- Pulmonary embolism (PE): thrombosis originating in venous system and embolizing to pulmonary arterial circulation; 1 case/1000 person y; 250,000/y (*Archives* 2003;163:1711)

Risk factors

- Virchow's triad for thrombogenesis

  stasis: bed rest, inactivity, CHF, CVA w/in 3 mo, air travel >6 h (*NEJM* 2001;345:779)

  injury to endothelium: trauma, surgery, prior DVT, inflammation, central catheter

  thrombophilia: APC resistance, protein C or S deficiency, APS, prothrombin gene mutation,↑ factor VIII, hyperhomocysteinemia, HIT, OCP, HRT, tamoxifen, raloxifene
- Malignancy (12% of “idiopathic” DVT/PE)
- History of thrombosis (greater risk of recurrent VTE than genetic thrombophilia)
- Obesity, smoking, acute infection, postpartum (*JAMA* 1997;277:642; *Circ* 2012;125:2092)

- Statin therapy ↑ risk (*NEJM* 2009;360:1851)

Thromboprophylaxis (*Chest* 2012;141:e195S, 227S, 278S)

Patient & situation	Prophylaxis
Low-risk med; same-day surg & <40 y	Early, aggressive ambulation
Minor surgery in mobile Pt	Mechanical Ppx
High-risk medical (eg, immobilized, h/o VTE, thrombophilia or cancer) Most surgery Pts	**UFH** 5000 U SC bid or tid, or **LMWH**, or fonda (if HIT ⊕), or mech Ppx (espec if high bleed risk)
High-risk surg (eg, trauma, recent stroke or spinal cord injury, h/o VTE or thrombophilia)	**[LMWH** or **UFH** SC**] + mech Ppx**
Orthopedic surgery	**LMWH** [or fonda, direct oral anticoag (qv) or warfarin (INR 2-3)] **+ mech Ppx** Start before or shortly after (<12 h) surgery & cont. up to **35 d** (hip) or 1**0-14 d** (knee). LMWH or fonda favored over UFH or VKA. Direct oral anticoagulants overall appear favorable vs LMWH.

For enoxaparin, 30 mg bid for highest risk or 40 mg qd for moderate risk or spinal/epidural anesth. Dose adjust: qd in CrCl <30 mL/min, ↑ 30% if BMI >40 (*Ann Pharmacother* 2009;43:1064).

- **Direct oral anticoagulants vs LMWH** (*Annals* 2012;156:710)

  Dabigatran (approved in Europe & Canada; 110 mg 1-4 h after surgery & hemostasis or 220 mg if not initiated on day of surgery; 220 mg qd maintenance) noninferior to LMWH after hip and knee surgery (*Lancet* 2007;370:949)

  Rivaroxaban (10 mg qd 6-10 h postop) ↓ VTE by ˜25-50% vs enox 40 mg qd, with ≈ bleeding after hip or knee replacement (*NEJM* 2008;358:2765 & 2776; *Lancet* 2009;373:1673)

  Apixaban (2.5 mg bid 12-24 h postop) ↓ VTE by ˜50% vs enox 40 mg qd, with ≈ bleeding after hip replacement (*NEJM* 2010;363:2487)

  Edoxaban (30 mg qd 6-24 h after surgery) ↓ VTE vs enox *20 mg qd,* but no comparison to standard dose enox (*Thromb Res* 2014;134:1198)

- Evolving role for Ppx in ambulatory cancer Pts w/ low bleeding risk and additional VTE risk factors (*NEJM* 2012;366:601). Khorana score (cancer site, plt & WBC counts, Hb, BMI) risk predictor (*Blood*

2008;111:4902). Semuloparin (ultra LMWH) ↓ VTE by ˜2/3 w/o ↑ major bleeding in Pts w/ met. or locally adv. cancer receiving chemo (*NEJM* 2012;366:601).

Clinical manifestations—DVT

- Calf pain, swelling (>3 cm c/w unaffected side), venous distention, erythema, warmth, tenderness, palpable cord, ⊕ Homan's sign (calf pain on dorsiflexion, seen in <5%)
- *Phlegmasia cerulea dolens:* massive proximal DVT → stagnant blood → edema, *cyanosis,* pain, compartment syndrome → can lead to limb loss or death
- 50% of Pts with sx DVT have asx PE
- Palpable tender superficial veins c/w superficial thrombophlebitis rather than DVT
- Popliteal (Baker's) cyst: related to knee pathology, may result in calf pain & may lead to DVT due to compression of popliteal vein

"Simplified Wells" Pretest Probability Scoring of DVT (*JAMA* 2006;295:199)

Clinical variable	Point score
◦ Active cancer (Rx ongoing or w/in 6 mo or palliative)	1
◦ Paralysis, paresis, or recent immobilization of lower extremities	1
◦ Recently bedridden for ≥3 d or major surgery w/in 12 wk	1
◦ Localized tenderness along distribution of deep venous system	1
◦ Entire leg swelling	1
◦ Calf ≥3 cm larger than asx calf (at 10 cm below tibial tuberosity)	1
◦ Pitting edema confined to sx leg	1
◦ Collateral superficial veins (nonvaricose)	1
◦ Previous DVT	1
◦ Alternative dx at least as likely as DVT	-2

Pretest Probability Assessment

Score ≤0	Score 1 or 2	Score ≥3
Low probability (5%)	Moderate probability (17%)	High probability (53%)

- For UE DVT, + 1 point each for venous cath, local pain, & unilateral edema, -1 if alternative dx. ≤1 = unlikely; ≥2 = likely. U/S if likely or if unlikely but abnl D-dimer (*Annals* 2014;160:451).

Diagnostic studies—DVT

- D-dimer: <500 helps r/o; ? use 1000 as threshold if low risk (*Annals* 2013;158:93)
- Compression U/S >95% Se & Sp for sx DVT (lower for asx DVT); survey whole leg rather than just proximal if ≥mod prob (*JAMA* 2010;303:438); venography rarely used

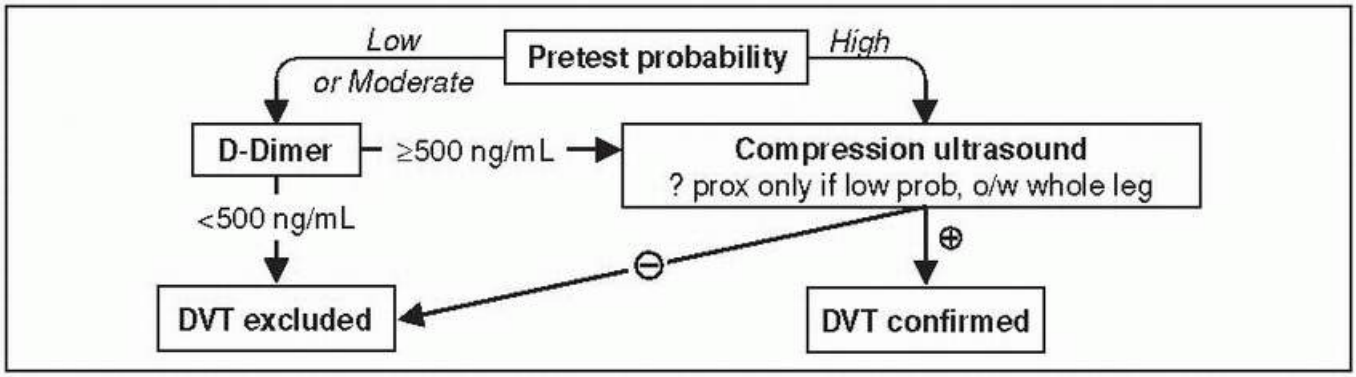


Figure 1-5 Approach to suspected DVT (*Chest* 2012;141:e351S)

Clinical manifestations—PE

- Dyspnea (73%), pleuritic chest pain (66%), cough (37%), hemoptysis (13%)
- ↑ RR (>70%), crackles (51%), ↑ HR (30%), fever, cyanosis, pleural friction rub, loud P_2
- *Massive:* syncope, HoTN, PEA; ↑ JVP, R-sided S3, Graham Steell (PR) murmur

Simplified Wells Pretest Probability Scoring for PE (*Annals* 2011;154:709)

- Prior PE or DVT
- Active cancer
- Immobilization (bed rest ≥3 d) or surgery w/in 4 wk
- Alternative dx less likely than PE
- Clinical signs of DVT
- HR >100 bpm
- Hemoptysis

Dichotomized Wells Probability Assessment

≤1 Variable = "Unlikely" (13% probability)

> 1 Variable = "Likely" (39% probability)

Diagnostic studies—PE (*NEJM* 2010;363:266)

- CXR (limited Se & Sp): 12% nl, atelectasis, effusion, ↑ hemidiaphragm, Hampton hump (wedge-shaped density abutting pleura); Westermark sign (avascularity distal to PE)
- ECG (limited Se & Sp): sinus tachycardia, AF; signs of RV strain → RAD, P pulmonale, RBBB, $S_IQ_{III}T_{III}$ & $TWIV_1$-V_4 (McGinn-White pattern; *Chest* 1997;111:537)
- ABG: hypoxemia, hypocapnia, respiratory alkalosis, ↑ A-a gradient (*Chest* 1996;109:78), 18% w/ room air P_aO_2 85-105 mmHg, 6% w/ nl A-a gradient (*Chest* 1991;100:598)
- D-dimer (*JAMA* 2015;313:1668): high Se, poor Sp (˜25%); ⊖ ELISA has >99% NPV ∴ use to r/o PE if "unlikely" pretest prob. (*JAMA* 2006;295:172) consider age-specific cutpoint: 500 if <50 y, 10× age if ≥50 y (*JAMA* 2014;311:1117)
- Echocardiography: useful for risk stratification (RV dysfxn), but not dx (Se <50%)
- V/Q scan: high Se (˜98%), low Sp (˜10%). Sp improves to 97% for high prob VQ. Use if pretest prob of PE high and CT not available or contraindicated. Can also exclude PE if low pretest prob, low prob VQ, but 4% false ⊖

(*JAMA* 1990;263:2753).

- **CT angiography** (CTA; see Radiology inserts; *JAMA* 2015;314:74): Se ~90% & Sp ~95% w/ MDCT (*NEJM* 2006;354:2317); PPV & NPV >95% if imaging concordant w/ clinical suspicion, ≤80% if discordant ([need to consider both); CT may also provide other dx
- Lower extremity compression U/S shows DVT in ~9%, sparing CTA, but when added to CTA, does not Δ outcomes (*Lancet* 2008;371:1343)

- Pulmonary angio: ? gold standard (morbidity 5%, mortality <0.5%), infrequently performed
- MR angiography: Se 84% (segmental) to 100% (lobar) (Lancet 2002;359:1643); if add MR venography, Se 92%, Sp 96% (Annals 2010;152:434)

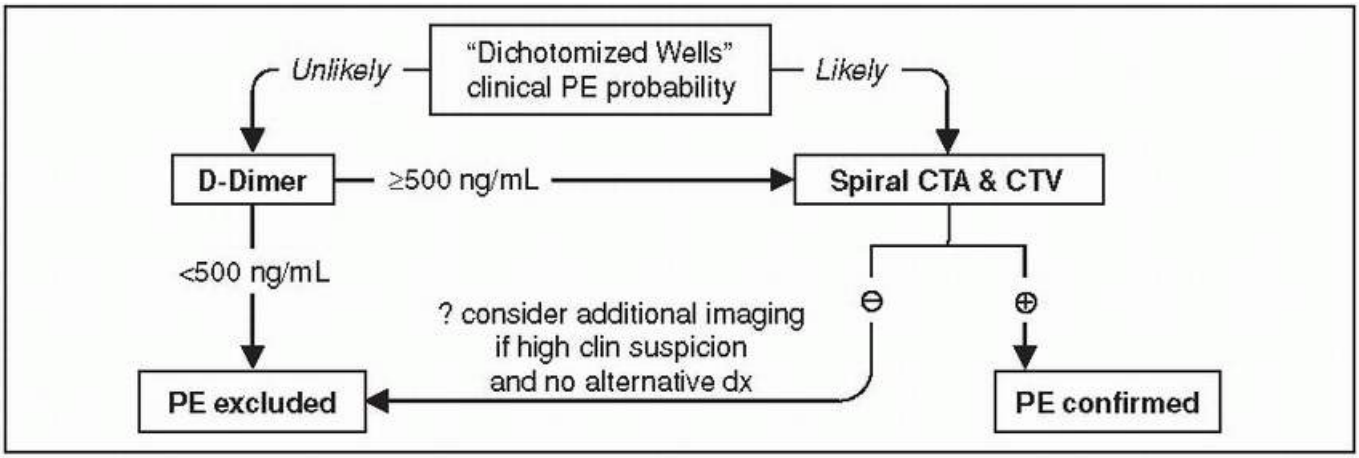


Figure 1-6 Approach to suspected PE using CTA

Workup for idiopathic VTE

- **Thrombophilia workup:** ✓ if ⊕ FH, may be helpful but consider timing as thrombus, heparin and warfarin Δ results. May not be helpful for Pt if will not change management (eg, plan for long-term anticoagulation regardless), although could be of use to relatives (*JAMA* 2005;293:2352; *Blood* 2008;112:4432; *Am J Med* 2008;121:458).
- **Malignancy workup:** 12% Pts w/ "idiopathic" DVT/PE will have malignancy; ageappropriate screening adequate; avoid extensive w/u (*NEJM* 1998;338:1169 & 2015;373:697)

Risk stratification for Pts with PE

- **Clinical:** hypotension and/or tachycardia (~30% mortality), hypoxemia
- **CTA:** RV / LV dimension ratio >0.9 (*Circ* 2004;110:3276)
- **Biomarkers:** ↑ troponin & ↑ BNP a/w ↑ mortality; w/ ⊖ Tn, decomp extremely unlikely (*Circ* 2002;106:1263 & 2003;107:1576; *Chest* 2015;147:685)
- **Echocardiogram:** RV dysfxn (even if normal troponin) (*Chest* 2013;144:1539)
- Simplified PE Severity Index: 0 RFs → 1.1% mort.; ≥1 → 8.9% mort (*Archives* 2010;170:1383) RFs: age >80 y; h/o cancer; h/o HF or lung disease; HR ≥110; SBP <100; S_aO_2 <90%

Whom to treat (*Lancet* 2012;379;1835; *Chest* 2012;141:e419S)

- **Superficial venous thrombosis:** elevate extremity, warm compresses, compression stockings, NSAIDs for sx. *Anticoag* if high risk for DVT (eg, ≥5 cm, proximity to deep vein ≤5 cm, other risk factors) for 4 wk as ~10% have VTE w/in 3 mo (*Annals* 2010;152:218).
- **LE DVT:** proximal → anticoag. If distal: anticoag if severe sx, o/w consider serial imaging over 2 wk and anticoag if extends (although if bleeding risk low, many would anticoag).
- **UE DVT:** anticoagulate (same guidelines as LE; *NEJM* 2011;364:861). If catheter-associated, need not remove if catheter functional and ongoing need for catheter.
- **PE:** anticoagulate

Anticoagulation options (*Chest* 2012;141:e419S; *JAMA* 2014;311:717)

- *Initiate immediately if high clinical suspicion or intermed but dx test results delayed for ≥4 h*
- Either (a) initial parenteral anticoag → long-term oral anticoagulant (eg, warfarin or Xa inhibitor) or (b) solely with an oral Xa inhibitor
- **LMWH** (eg, enoxaparin 1 mg/kg SC bid *or* dalteparin 200 IU/kg SC qd)

  Preferred over UFH (espec in *cancer*) except: renal failure (CrCl <25), ? extreme obesity, hemodynamic instability or bleed risk (*Cochrane* 2004;CD001100)

  No need to monitor anti-factor Xa unless concern re: dosing (eg, renal insuffic.)

  Attractive option as outPt bridge to long-term oral anticoagulation
- If cancer, LMWH ↓ recur. & mort. c/w UFH & warfarin (*NEJM* 2003;349:146; *Lancet Oncol* 2008;9:577; *JAMA* 2015;314:677); ✓ head CT for brain mets if melanoma, renal, thyroid, chorioCA
- **Fondaparinux:** 5-10 mg SC qd (*NEJM* 2003;349:1695); use if HIT ⊕; avoid if renal failure
- DVT & low-risk PE can be treated completely as outPt (*Lancet* 2011;378:41)
- **IV UFH:** 80 U/kg bolus → 18 U/kg/h → titrate to PTT 1.5-2.3 × cntl (eg, 60-85 sec); preferred option when contemplating thrombolysis or catheter-based Rx (qv)
- IV Direct thrombin inhibitors (eg, argatroban, lepirudin) used in HIT ⊕ Pts
- **Warfarin** (goal INR 2-3): start same day as parenteral anticoag unless instability and ? need for lytic, catheter-based Rx or surgery; overlap ≥5 d w/ parenteral anticoag & until INR ≥2 × ≥24 h
- **Oral Xa inhibitor:** effect wears off w/in 24 h, but not easily immediately reversed

  Can give as sole anticoag (nb, initial doses higher than for AF): **rivaroxaban** (15 mg bid for 1st 3 wk → 20 mg/d) as good/better than LMWH → warfarin in preventing recurrent VTE, ↓ bleeding (*NEJM* 2010;363:2499 & 2012;366:1287); **apixaban** (10 mg bid × 7 d → 5 bid) ≈ LMWH → warfarin in preventing recurrent VTE, ↓ bleeding (*NEJM* 2013;369:799)

  Can initiate after ≥5 d of parenteral anticoag (1st dose when d/c IV UFH or w/in 2 h before when next LMWH dose would have been due): both **dabigatran** (150 mg bid) & **edoxaban** (60 mg qd) ≈ warfarin but w/ ↓ bleeding (*NEJM* 2009;361:2342 & 2013;369:1406)

Systemic thrombolysis (*Chest* 2012;141:e419S)

- Typically TPA 100 mg over 2 h or wt-adjusted TNK bolus

- Indications & efficacy below; risk of ICH ~1.5%, ↑ w/ age; see contraindications in "ACS"
- **Massive PE** (hemodynamic compromise): ↓ death and recurrent PE each by ~50% (*Circ* 2004;110:744; *JAMA* 2014;311:2414; *EHJ* 2015;36:605) & lower PVR long term (*JACC* 1990;15:65)
- **Submassive PE** (hemodyn. stable but RV dysfxn on echo or enlargement on CTA, or ? marked dyspnea or severe hypoxemia): ↑ death & ↑ bleeding; may consider if low bleed risk (see lytic contra-indic.; *EHJ* 2015;36:605). Benefit/risk may be more favorable if <75 y (*NEJM* 2014;370:1402; *JAMA* 2014;311;2414). Some centers prefer catheter-directed Rx (qv).
- **Moderate PE w/ large clot burden** (≥2 lobar arteries or main artery on CT or high prob VQ w/ ≥2 lobes w/ mismatch): *low-dose lytic* (50 mg if ≥50 kg or 0.5 mg/kg if >50 kg; for both 10 mg bolus → remainder over 2 h) ↓ pulm HTN w/ ≈ bleeding vs heparin alone; await further validation (*Am J Cardiol* 2013;111:273)
- **DVT:** consider if all are present (a) acute (< 14 d) & extensive (eg, iliofemoral), (b) severe symptomatic swelling or ischemia (phlegmasia cerulea dolens), (c) catheter-directed Rx not available, and (d) low bleeding risk

Mechanical intervention

- **Catheter-directed therapy** (fibrinolytic & thrombus fragmentation/aspiration)

  Consider if extensive DVT (see above) and to ↓ post-thrombotic synd (*Lancet* 2012;379:31)

  Consider if PE w/ hemodyn. compromise or high risk & not candidate for systemic lysis or surgical thrombectomy (*Circ* 2011;124:2139). Preferred to systemic lytic by some centers.

  U/S-assisted → improves hemodynamics & RV fxn vs anticoag alone (*EHJ* 2015;36:597)
- **Thrombectomy:** if large, proximal PE + hemodynamic compromise + contra. to lysis; consider in experienced ctr if large prox. PE + RV dysfxn (*J Thorac CV Surg* 2005;129:1018)
- **IVC filter:** use instead of anticoagulation if latter contraindicated

  No benefit to adding to anticoag (including in submassive) (*JAMA* 2015;313:1627)

  Consider removable filter for temporary indications

  Complications: migration, acute DVT, ↑ risk of recurrent DVT & IVC obstruction (5-18%), which may lead to worsening LE sx (*Archives* 1992;152:1985)

Duration of full-intensity anticoagulation

- Superficial venous thrombosis: 4 wk
- 1st prox DVT *or* PE 2° reversible/time-limited risk factor *or* distal DVT: 3-6 mo
- 1st *unprovoked* prox DVT/ PE: ≥3 mo, then reassess; benefit to prolonged Rx (see below). Consider bleeding risk, Pt preference and intensity of extended Rx.
- 2nd VTE event or cancer: indefinite (or until cancer cured) (*NEJM* 1997;336:393 & 2003;348:1425)
- Does *not* appear that can rely on D-dimer testing to guide d/c (*Annals* 2015;162:27)

Extended antithrombotic strategies (*JAMA* 2015;314:72)

- After ≥6 mo of anticoag, following strategies have been compared w/ *no extended* Rx*:*
- Full-dose dabigatran, rivaroxaban, or apixaban: 80-90% ↓ recurrent VTE, 2-5× bleeding, but no signif excess

in major bleeding (*NEJM* 2010;363:2499; 2013;368:699 & 709)

- Full-dose warfarin: 85% ↓ reduction in recurrent VTE (*JAMA* 2015;314:31)
- Low-intensity warfarin (INR 1.5-2.0): 64% ↓ reduction in recurrent VTE (*NEJM* 2003;348:1425)
- Low-intensity apixa (2.5 mg bid): 80% ↓ recur. VTE, w/o signif ↑ bleeding (*NEJM* 2013;368:699)
- Aspirin: 32% ↓ recurrent VTE (*NEJM* 2012;366:1959 & 367:1979)

Other therapeutic interventions

- Early ambulation
- For DVT: fitted graduated compression stockings (min 20-30 mmHg → 30-40 mmHg) for sx & to ↓ risk of postthrombotic synd (occurs in 23-60%; *J Thromb Thrombolysis* 2009;28:465)
- Leg elevation and exercise (use of calf muscle pump) also may be helpful
- Anticoag teaching: avoidance of high-risk activities, med alert bracelet, dietary instructions

Complications & prognosis

- Post-thrombotic syndrome (23-60%): thrombosis → injury to vein/valves → pain, edema, venous ulcers (*J Thromb Thrombolysis* 2009;28:465)
- Recurrent VTE: 1%/y (after 1st VTE) to 5%/y (after recurrent VTE) after only 6 mo of Rx: 5%/y & > 10%/y, respectively

  predictors: abnl D-dimer 1 mo after d/c anticoag (*NEJM* 2006;355:1780); ⊕ U/S after 3 mo of anticoag (*Annals* 2002;137:955); thrombin generation >400 nM (*JAMA* 2006;296:397)
- Chronic thromboembolic PHT after acute PE ~3.8% (*NEJM* 2004;350:2257), consider thromboendarterectomy
- Mortality: ~10% for DVT and ~10-15% for PE at 3-6 mo (*Circ* 2008;117:1711)

PULMONARY HYPERTENSION (PHT)

PA *mean pressure ≥25 mmHg at rest*

Pathobiology (*NEJM* 2004;35:1655)

- Smooth muscle & endothelial cell proliferation; mutations in bone morphogenic protein receptor 2 (*BMPR2*) in ~50% familial & ~26% sporadic cases of IPAH (*NEJM* 2001;345:319)
- Imbalance between vasoconstrictors and vasodilators

  ↑ vasoconstrictors: thromboxane A_2 (TXA_2), serotonin (5-HT), endothelin-1 (ET-1)

  ↓ vasodilators: prostacyclin (PGI2), nitric oxide (NO), vasoactive peptide (VIP)
- *In situ* thrombosis: ↑ TXA_2, 5-HT, PAI-1; ↓ PGI_2, NO, VIP, tissue plasminogen activator

Etiologies of Pulmonary Hypertension (Revised WHO Classification)	
Pulmonary arterial HTN	• Idiopathic (IPAH): mean age of onset 36 y (♂ older than ♀); ♀:♂= ~2:1,

(PAH) (group 1)	usually mild ↑ in PAP • Familial (FPAH) • Associated conditions (APAH) Connective tissue disorders: CREST, SLE, MCTD, RA, PM, Sjögren Congenital: L→R shunts: ASD, VSD, PDA, 1° PHT of newborn Portopulmonary HTN (? 2° vasoactive substances not filtered in ESLD; ≠ hepatopulmonary syndrome) HIV; drugs & toxins: anorexic agents, rapeseed oil, L-tryptophan • Pulmonary veno-occlusive disease: ? 2° chemo, BMT; orthopnea, pl eff, nl PCWP; art vasodil. *worsen* pulm edema (*AJRCCM* 2000;162:1964) • Pulmonary capillary hemangiomatosis
Left heart disease (group 2)	• Left atrial or ventricular (diastolic or systolic) dysfunction • Left-sided valvular heart disease (eg, MS/MR > AS/AR) • Congenital: left-sided inflow/outflow obstruction, CMP
Lung diseases and/or chronic hypoxemia (group 3)	• COPD • ILD • Sleep apnea • Alveolar hypoventilation (eg, NM disease) • Chronic hypoxemia (eg, high altitude) • Developmental abnormalities
Chronic thrombo-embolic dis (group 4)	• Prox or distal PEs; ~½ w/o clinical h/o PE (*Circ* 2014;130:508) • Nonthrombotic emboli (tumor, foreign body, parasites)
Miscellaneous (group 5) (*Circ* 2013;62:25S)	• Sarcoidosis, histiocytosis X, LAM, schistosomiasis • Metab: thyroid, glycogen storage, Gaucher • Heme: chronic hemolytic anemia, myeloprolif d/o, splenectomy • Other: compression of pulm vessels (adenopathy, tumor, fibrosing mediastinitis, histoplasmosis, XRT); HHT (multifactorial)

Clinical manifestations

- Dyspnea, exertional syncope (hypoxia, ↓ CO), exertional chest pain (RV ischemia)
- Symptoms of R-sided CHF (eg, peripheral edema, RUQ fullness, abdominal distention)
- WHO class: I = asx w/ ordinary activity; II = sx w/ ord. activ.; III = sx w/ min activ.; IV = sx at rest

Physical exam

- PHT: prominent P_2, R-sided S4, RV heave, PA tap & flow murmur, PR (Graham Steell), TR
- ± RV failure: ↑ JVP, hepatomegaly, peripheral edema

Diagnostic studies & workup (*Circ* 2014;130:1820)

- *IPAH yearly incidence 1-2 per million, ∴ r/o 2° causes*

- High-res chest CT: dil. & pruning of pulm arteries, ↑ RA and RV; r/o parenchymal lung dis.
- ECG: RAD, RBBB, RAE ("P pulmonale"), RVH (Se 55%, Sp 70%)
- PFTs: disproportionate ↓ $D_L$co, mild restrictive pattern; r/o obstructive & restrict. lung dis.
- ABG & polysomnography: ↓ P_aO_2 and S_aO_2 (espec w/ exertion), ↓ P_aCO_2, ↑ A-a gradient; r/o hypoventilation and OSA
- TTE: ↑ RVSP (but estimate over/under by ≥10 mmHg in ½ of PHT Pts; *Chest* 2011;139:988)

  ↑ RA, RV (RV:LV area >1) and PA size; TR, PR

  ↑ RVSP → interventricular septum systolic flattening ("D" shape)

  ↑ RAP → interatrial septum bowing into LA

  ↓ RV systolic fxn: TAPSE (tricuspid annular plane systolic excursion) < 1.6 cm; lateral-septal tissue-Doppler imaging disparity (reflecting relatively more systolic dysfxn of RV lateral wall vs septum, which is shared with LV)

  ↑ PA impedance ↑ RVOT Doppler notching

  r/o LV dysfxn, MV or AoV disease, and congenital heart disease
- RHC: ↑ RA, RV, & PA pressures; ✓ L-sided pressures and for shunt if PAH: nl PCWP, ↑ transpulm gradient (mean PAP-PCWP > 12-15), ↑ PVR, ± ↓ CO if 2° to L-heart disease: PCWP (or LVEDP) > 15; if PVR nl → "passive PHT"; PVR >240 suggests mixed picture: if ↓ PCWP → ↓ PVR, then "reactive" PHT; if no Δ, then "fixed"

- CTA (large/med vessel), V/Q scan (small vessel to r/o CTEPH), ± pulmonary angiogram: r/o PE and chronic thromboembolic disease
- Vasculitis labs: ANA (˜40% ⊕ in PAH), RF, anti-Scl-70, anticentromere, ESR
- LFTs & HIV: r/o portopulmonary and HIV-associated PAH
- 6-min walk test (6MWT) or cardiopulmonary exercise testing to establish fxnl capacity

Differentiating Left Heart Disease from Alternative PHT Etiologies

Feature	Favors Left Heart Disease	Favors Alternative Etiology
History	Prior MI, CMP,AoV or MV disease, CV risk factors (HTN, diabetes), ↑ age	Family hx PHT, connective tissue disorder, pulm, liver or hematologic disease, HIV, h/o VTE
PEx	L-sided S3, S4 L-sided murmurs Displaced apical impulse Coarse rales	Cyanosis, clubbing Fine rales; signs of COPD Raynaud's, sclerodactyly, telangiectasia Splenomegaly, spider angiomata
ECG	Q waves, LVH, LBBB	Isolated RAE, RVH, $S_IQ_{III}T_{III}$ pattern

Echo	LV systolic or diastolic dysfxn LVH, ↑ LA size ≥Moderate MV or AoV disease	Isolated RV or RA enlargement Interventricular septum systolic flattening and/or interatrial septum bowing into LA ↓ RV systolic fxn
RHC	↑ L-sided filling pressures Abrupt ↑ PCWP (to > 20-25) w/ exercise or volume loading	PCWP <15 mmHg Exercise PCWP <20-25 mmHg

Treatment (*JACC* 2013;62:25S & 2015;65:1976)

- Principles

  1) prevent and reverse vasoactive substance imbalance and vascular remodeling

  2) prevent RV failure: ↓ wall stress (↓ PVR, PAP, RV diam); ensure adeq. systemic DBP

- **Supportive**

  Oxygen: maintain S_aO_2 >90-92% (reduces vasoconstriction)

  Diuretics: ↓ RV wall stress and relieve RHF sx; *gentle* b/c RV is preload dependent

  Digoxin: control AF, ? counteract neg. inotropic effects CCB

  Dobutamine and inhaled NO or prostacyclin for decompensated PHT

  Anticoagulation: ↓ VTE risk of RHF; ? prevention of *in situ* microthrombi; ? mortality benefit even if in NSR, no RCTs (*Circ* 1984;70:580; *Chest* 2006;130:545)

  Supervised exercise training (*Eur Respir J* 2012;40:84)

- **Vasodilators** (right heart catheterization prior to initiation) *acute vasoreactivity test:* use inhaled NO, adenosine or prostacyclin to identify Pts likely to have a long-term response to oral CCB (⊕ vasoreactive response defined as ↓ PAP ≥10 mmHg to a level <40 mmHg with ↑ or stable CO); ˜10% Pts are acute responders; no response → still candidates for other vasodilators (*NEJM* 2004;351:1425)

Vasoactive agents	Comments (data primarily in Group 1 PAH)
Oral CCB Nifedipine, diltiazem	If ⊕ acute vasoreactive response; <½ will be long-term responder (NYHA I/II & near-nl hemodynamics) & have ↓ mortality. Side effects: HoTN, lower limb edema (*NEJM* 1992;327:76; *Circ* 2005;111:3105).
IV Prostacyclin Epoprostenol (Flolan)	Vasodilation, ↓ plt agg, ↓ smooth muscle proliferation; benefits ↑ w/ time (? vascular remodeling). ↑ 6MWT, ↑ QoL, ↓ mortality. Side effects: HA, flushing, jaw/leg pain, abd cramps, nausea, diarrhea, catheter infxn (*NEJM* 1996;334:296 & 1998:338:273; *Annals* 2000;132:425).
Prostacyclin analogues Iloprost (inhaled) Treprostinil (IV, inh, SC) Beraprost (PO)	Same mechanism as prostacyclin IV, but easier to take, ↓ side effects, and w/o risk of catheter infxn, ↓ sx, ↑ 6MWT; trend to ↓ clinical events w/ iloprost but not treprostinil. Beraprost w/o sustained outcome improvement (n/a in U.S.) (*NEJM* 2002;347:322; *AJRCCM* 2002;165:800).

Endothelin receptor antagonists (ERAs) Bosentan, ambrisentan, macitentan	↓ Smooth muscle remodeling, vasodilation, ↓ fibrosis, ↓ sx, ↑ 6MWT, ↓ worsening PAH or need for prostanoids w/ trend for ↓ PAH mortality (w/ macitentan). Side effects: ↑ LFTs, headache, anemia, edema, teratogen (*NEJM* 2002;346:896; *JACC* 2005;46:529; *Circ* 2008;117:3010; *NEJM* 2013;369:809).
PDE-5 Inhibitor Sildenafil, tadalafil	↑ cGMP → vasodilation, ↑ smooth muscle proliferation, ↓ sx, ↑6MWT, no data on clinical outcomes. Low side-effect profile: HA, vision Δ's, sinus congestion (*NEJM* 2009;361:1864).
Soluble guanylate cyclase stimulator Riociguat	NO-independent ↑ cGMP → vasodilation, ↑ smooth muscle proliferation, ↓ sx, ↑ 6MWT in PAH; ↓ sx, ↓ PVR, ↑ 6MWT in CTEPH (*NEJM* 2013;369:319 & 330)

- Up front combination Rx (tadalafil + ambrisentan vs monotherapy): ↓ sx, ↓ NT-BNP, ↑ 6MWT, ↓ hospitalizations (*NEJM* 2015;373:834)
- Treat underlying causes of 2° PHT; can use vasodilators, although little evidence beyond riociguat use for CTEPH as described above
- Refractory PHT:

  balloon atrial septostomy: R→ L shunt causes ↑ CO, ↓ S_aO_2, net ↑ tissue O_2 delivery lung transplant (single or bilateral); heart-lung needed if Eisenmenger physiology

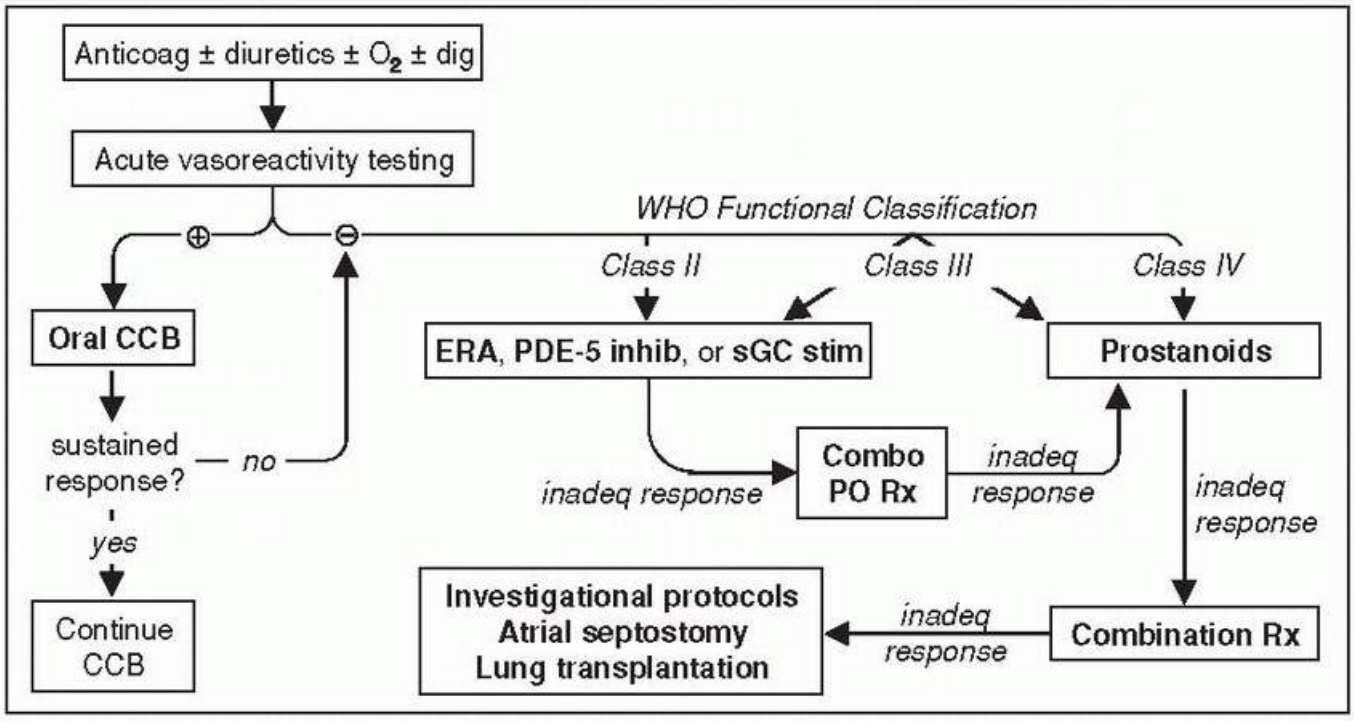


Figure 1-7 Treatment of PAH (modified from *JACC* 2009;54:S78)

Management of ICU patient

- Avoid overly aggressive volume resuscitation
- Caution with vasodilators if any L-sided dysfunction
- May benefit from inotropes/chronotropes
- Mechanical RV support (RVAD, ECMO) (*Circ* 2015;132:526)
- Consider fibrinolysis if acute, refractory decompensation (eg, TPA 100 mg over 2 h)

Prognosis

- Median survival after dx ~2.8 y; PAH (all etiologies): 2-y 66%, 5-y 48% (*Chest* 2004;126:78-S)
- Poor prognostic factors: clinical evidence of RV failure, rapidly progressive sx, WHO (modified NYHA) class IV, 6MWT <300 m, peak VO_2 <10.4 mL/kg/min, ↑ RA or RV or RV dysfxn, RA >20 or CI <2.0, ↑ BNP (*Chest* 2006;129:1313)
- Lung transplant: 1-y survival 66-75%; 5-y survival 45-55% (*Chest* 2004;126:63-S)

Arrhythmias

BRADYCARDIA AND AV BLOCK

BRADYCARDIAS

Sinus bradycardia (SB) (*NEJM* 2000;342:703)

- Etiologies: **meds** (incl βB, CCB, amio, Li, dig), → **vagal tone** (incl. in athletes, sleep, IMI), **metabolic** (hypoxia, sepsis, myxedema, hypothermia, ↓ glc), OSA, ↑ ICP
- Treatment: if no sx, none; atropine, β_1 agonists or long-term permanent pacing if sx
- Most common cause of sinus pause is *blocked premature atrial beat*

Sick sinus syndrome (SSS)

- Features may include: periods of unprovoked SB, SA arrest, paroxysms of SB and atrial tachyarrhythmias ("tachy-brady" syndrome), chronotropic incompetence w/ ETT
- Treatment: meds alone usually fail (adeq. control of tachy → unacceptable brady); usually need **combination of meds** (βB, CCB, dig) for tachy & **PPM** for brady

Pseudobradycardia

- Intermittent PVCs (with low stroke volume and hence low pulse wave) followed by compensatory pause can cause ascertainment of HR by palpation of radial pulse to be artifactually low

AV BLOCK AND AV DISSOCIATION

AV Block

Type	Features
1°	Prolonged PR (>200 ms), all atrial impulses conducted (1:1)
2° Mobitz I (Wenckebach)	Progressive ↑ PR until impulse not conducted (↑ "grouped beating") Due to **AV node** conduction delay: ischemia (IMI), inflammation (myocarditis, MV surgery), high vagal tone (athletes), drug-induced QRS duration most often normal AVB usually worsens w/ carotid sinus massage, improves w/ atropine & exercise Often paroxysmal/nocturnal/asymptomatic; no Rx required
2° Mobitz II	Occasional or repetitive blocked impulses w/ consistent PR interval. Nb, do not confuse with APBs in bigeminal pattern; to dx AVB, atrial rate should be *regular* and P waves should be the *same.* Due to **His-Purkinje** conduction delay: ischemia (AMI), degeneration of conduction system, infiltrative disease, inflammation/valve surgery QRS duration most often prolonged AVB usually improves w/ carotid sinus massage, worsens w/ atropine & exercise (both of which should be *avoided* if dx suspected) Risk of progression to 3° AVB. Zoll at bedside when recognized; temp pacing wire or PPM often required.

3° (complete)	No AV conduction, with ventricular rhythm slower than atrial rhythm Escape, if present is regular and can be narrow (jxnal) or wide (vent.) Urgent temporary pacing as bridge to permanent pacing is appropriate in most scenarios, especially when syncope present

Nb, if 2:1 block, cannot distinguish type I vs II 2° AVB (no chance to observe PR prolongation); usually categorize based on other ECG & clinical data. High-grade AVB usually refers to block of ≥2 successive impulses. All categories above assume SR in atrium, criteria do not apply during rapid atrial rates, such as in atrial flutter or tachycardia.

AV dissociation

- *Default:* slowing of SA node allows subsidiary pacemaker (eg, AV junction) to take over
- *Usurpation:* acceleration of subsidiary pacemaker (eg, AV junctional tach, VT)
- *3° AV block:* atrial pacemaker unable to capture ventricles, subsidiary pacemaker emerges; distinguish from *isorhythmic dissociation* (A ≈V rate, some P waves nonconducting)

Temporary pacing wires

- Consider w/ bradycardia with hemodyn instability or unstable escape rhythm when perm pacer not readily available. Risks: RV perf, VT, PTX, CHB if existing LBBB, etc.
- Consider instead of PPM for sx bradycardia due to reversible cause (βB/CCB O/D, Lyme, myocarditis, SBE, s/p cardiac surgery/trauma), TdP, acute MI (sx brady, high-grade AVB)

SUPRAVENTRICULAR TACHYCARDIAS

PALPITATIONS

Etiologies

- PACs, PVCs; SVT, AF, VT, respiratory sinus arrhythmia; pauses; noncardiac

Workup

- History: duration & frequency; initiating & aggravating factors: exercise, alcohol, stimulants (caffeine, pseudoephedrine, other prescription & recreational drugs); h/o presyncope or syncope; FHx of arrhythmia, CMP, SCD
- Structural evaluation w/ echo; consider ETT if exercise-induced or other RF; TFTs
- Ambulatory cardiac monitoring: *must monitor during symptoms to diagnose!* Holter (worn continuously): if sx typically occur within a 24-48-hr period Looping event monitor (worn continuously): if sx fleeting Nonlooping event monitor (put on during sx): if rarer episodes lasting minutes

Treatment (for SVT and VT, see respective sections)

- Simple ectopy in structurally normal heart: reassurance, βB, CCB. If refractory, frequent sx with poor QoL, antiarrhythmic drug, such as flecainide, can be tried in consultation w/ electrophysiologist. Rarely catheter ablation for frequent PVCs.

- If NICM and > 13% PVCs, elim of ectopy w/ catheter ablation can significantly ↑ EF (*JACC* 2013;62:1195). However, risk of *developing* CMP due to frequent PVCs not established.

SUPRAVENTRICULAR TACHYCARDIAS (SVTS)

Arise above the ventricles, ∴ ***narrow QRS*** *unless aberrant conduction or pre-excitation*

Common Etiologies of SVT (*NEJM* 2006;354:1039 & 2012;367:1438)

	Type	Features
Atrial	Sinus tachycardia (ST)	Caused by pain, fever, hypovolemia, hypoxia, anemia, anxiety, β-agonists, etc.
	Atrial tachycardia (AT)	Originate at site in atria other than SA node. Seen w/ CAD, COPD, ↑ catechols, EtOH, dig.
	Multifocal atrial tachycardia (MAT)	↑ automaticity at multiple sites in the atria. Seen with underlying pulmonary disease.
	Atrial flutter (AFL)	Macroreentry, usually w/in right atrium
	Atrial fibrillation (AF)	Chaotic atrial activation and rapid, irregular bombardment of AVN
	AV nodal reentrant tach (AVNRT)	Reentrant circuit using dual pathways w/in AVN
	AV reciprocating tachycardia (AVRT)	Reentrant circuit using AVN antegrade and accessory pathway retrograde. When in sinus rhythm may show pre-excitation (WPW) or not (concealed accessory pathway).
AV Jxn	Paroxysmal junctional reciprocating tachycardia (PJRT)	Reentry using AVN & slowly conducting concealed posterosept acc path. More common in peds, at times w/ tachy-induced CMP.
	Nonparoxysmal junctional tachycardia (NPJT)	↑ jxnal automaticity. May see retrograde P's & AV dissoc. A/w myo/endocarditis, cardiac surg, IMI, dig.

Diagnosis of SVT Type (*NEJM* 2006;354:1039 & 2012;367:1438)

Onset	Abrupt on/off argues against sinus tachycardia

Rate	Not dx as most can range from 140-250 bpm, *but:* ST usually <150; AFL often conducts 2:1 → vent. rate 150; AVNRT & AVRT usually >150
Rhythm	Irregular → AF, AFL w/ variable block, or MAT
P wave	Long RP: ST (P same as sinus), AT, MAT (≥3 morphologies), PJRT Short RP, P inverted in inf. leads → *retrograde* atrial activation via AVN AVNRT: buried in or distort terminal portion of QRS (pseudo-RSR' in V_1) AVRT: slightly after QRS (RP interval > 100 ms favors AVRT vs AVNRT) NPJT: either no P wave or retrograde P wave similar to AVNRT *Fibrillation or no P waves* → AF *Saw-toothed "F" waves* (best seen in inferior leads & V_1) → AFL
Response to vagal stim. or adenosine	Slowing of HR often seen with ST, AF, AFL, AT, whereas reentrant rhythms (AVNRT, AVRT) may abruptly terminate (classically w/ P wave after last QRS) or no response. Occ AT may terminate. AFL & AF → ↑ AV block → unmasking of "F" waves or fibrillation

Short RP: P wave closer to preceding than following QRS (ie, RP < PR). Long RP: P wave closer to following than preceding QRS (ie, PR < RP).

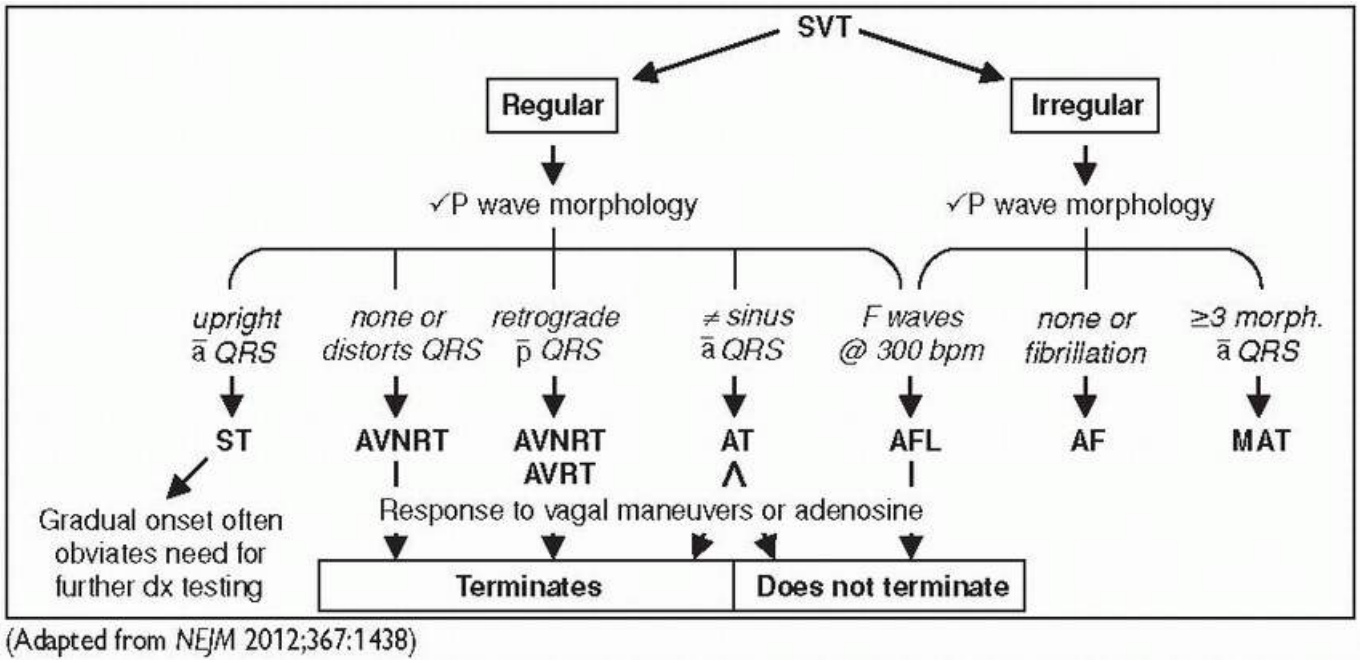


Figure 1-8 Approach to SVT

Treatment of SVT

Rhythm	Acute treatment	Long-term treatment
Unstable	**Cardioversion** per ACLS	n/a

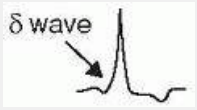
ST	Treat underlying stressor(s)	n/a
AT	βB, CCB or amiodarone; ? vagal maneuvers or adenosine	βB or CCB, ± antiarrhythmics, possibly radiofrequency ablation (RFA)
AVNRT or AVRT	**Vagal maneuvers** **Adenosine** (caution in AVRT*) **CCB** or βB	*For AVNRT* (*see next section for AVRT*): **RFA.** CCB or βB (chronic or prn) ± Class IC antiarrhythmics (if nl heart)
NPJT	**CCB, βB, amiodarone**	Rx underlying dis. (eg, dig tox, ischemia)
AF	**βB, CCB, digoxin, AAD**	See "Atrial Fibrillation"
AFL	**βB, CCB, digoxin, AAD**	RFA; βB or CCB ± antiarrhythmics
MAT	CCB or βB if tolerated	Treat underlying disease process AVN ablation + PPM if refractory to meds

*Avoid adenosine & nodal agents if accessory pathway + preexcited tachycardia, see below (*JACC* 2003;42:1493)

- *Catheter ablation:* high overall success rate (AFL/AVNRT ˜95%, AVRT ˜90%, AF ˜80%) Complications: stroke, MI, bleeding, perforation, conduction block (*JAMA* 2007;290:2768)

ACCESSORY PATHWAYS (WOLFF-PARKINSON-WHITE)

Definitions

- **Accessory pathway** (bypass tract) of conducting myocardium connecting 

atria & ventricles, allowing impulses to bypass normal AVN delay
- **Preexcitation (WPW) pattern:** ↓ PR interval, ↑ QRS width w/ δ wave (slurred onset, *can be subtle*), ST & Tw abnl (can mimic old IMI);

  only seen w/ pathways that conduct antegrade (if pathway only conducts retrograde then ECG will be normal during SR; "concealed" bypass tract)

  PAC can exaggerate preexcitation if AV node conduction slowed
- **WPW syndrome:** accessory pathway + paroxysmal tachycardia

Classic tachycardias of WPW

- **Orthodromic AVRT:** *narrow-complex* SVT (typically), conducting ↑ AVN & ↑ accessory pathway; requires retrograde conduction and ∴ can occur w/ concealed bypass tracts
- **Antidromic AVRT** (less common): *wide-complex* regular tachycardia, conducting ↓ accessory pathway & ↑

AVN. Can meet many ECG morphology criteria for VT. Requires antegrade conduction and ∴ should see WPW pattern during SR.

- **AF** w/ rapid conduction down accessory pathway; ∴ wide-complex irregular SVT; requires antegrade conduction; ∴ should see WPW pattern in SR. Rarely can degenerate into VF.

Treatment

- **AVRT:** vagal, βB; caution w/ adenosine (can precip. AF); *have defibrillator ready*
- **AF/AFL** w/ conduction down accessory pathway: need to Rx arrhythmia *and* ↑ pathway refractoriness; use **procainamide**, **ibutilide**, or DCCV; avoid CCB & βB, dig/adenosine (can ↓ refractoriness of pathway → ↑ vent. rate ↑ VF)
- **Long term:** Rx sx tachycardias w/ RFA, antiarrhythmics (IA, IC) if not candidate for RFA.

  Consider RFA if asx but AVRT or AF inducible on EPS (*NEJM* 2003;349:1803) or if rapid conduction possible (✓ w/ EPS if preexcitation persists despite exercise testing).

  Risk of SCD related to how short RR interval is in AF and # of accessory pathways present. Exercise testing to look for loss of pre-excitation can be used as a proxy for short RR interval in AF: if pathway still present at peak exercise, more concerning.

ATRIAL FIBRILLATION

Classification (*Circ* 2014;130:2071)

- **Paroxysmal** (terminates spontaneously or w/ Rx w/in 7 d) vs **persistent** (sustained >7 d) vs **long-standing persistent** (>1 y) vs **permanent** (no plan to restore or maintain SR)
- **Nonvalvular** (AF absent rheumatic MS, prosthetic valve or mitral valve repair) vs **valvular**
- **Lone AF** = age <60 y and w/o clinical or echo evidence of cardiac disease (including HTN)

Pathophysiology

- Disorganized atrial electrical activity → ineffective atrial mechanical contraction
- For paroxysmal AF, >90% triggered by rapid firing in pulmonary veins (*NEJM* 1998;339:659)

Epidemiology and etiologies (*Annals* 2008;149:ITC5-2)

- 1-2% of pop. has AF (8% of elderly); lifetime risk 25%; mean age at presentation ~75 y
- Acute (up to 50% w/o identifiable cause)

  Cardiac: HF, myo/pericarditis, ischemia/MI, hypertensive crisis, cardiac surgery

  Pulmonary: acute pulmonary disease or hypoxia (eg, COPD flare, PNA), PE, OSA

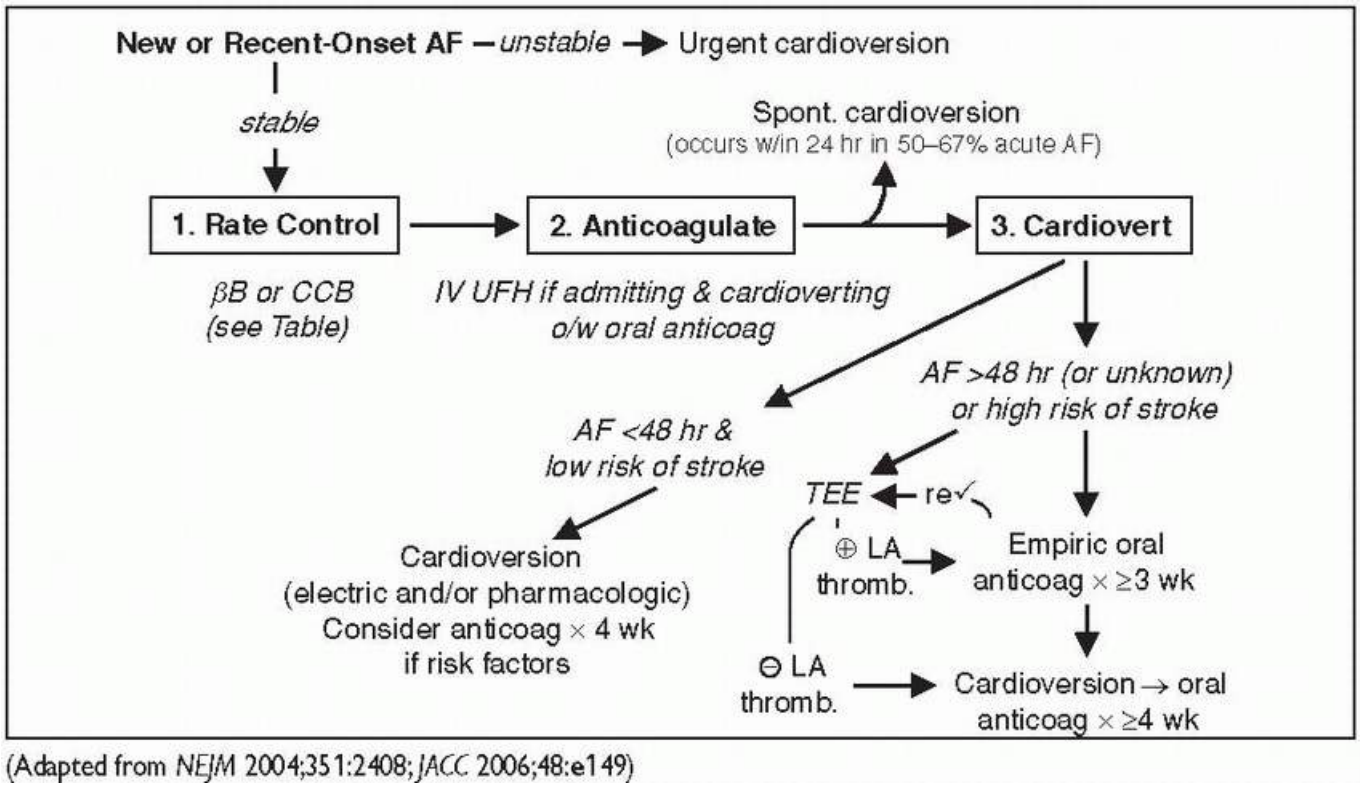
  Metabolic: high catecholamine states (stress, infection, postop, pheo), thyrotoxicosis

  Drugs: alcohol (“holiday heart”), cocaine, amphetamines, theophylline, caffeine

  Neurogenic: subarachnoid hemorrhage, ischemic stroke
- Chronic: ↑ age, HTN, ischemia, valve dis. (MV, TV, AoV), CMP, hyperthyroidism, obesity

Evaluation

- H&P, ECG, CXR, TTE (LA size, thrombus, valves, LV fxn, pericardium), K, Mg, FOBT before anticoag, TFTs; r/o MI not necessary unless other ischemic sx



(Adapted from *NEJM* 2004;351:2408; *JACC* 2006;48:e149)

Figure 1-9 Approach to acute AF

Rate control

- If sx, goal HR <80; if asx & EF >40%, goal HR <110 at rest (*NEJM* 2010;362:1363)
- AV node ablation + PPM if pharmacologic Rx inadequate (*NEJM* 2001;344:1043; 2002;346:2062)

Rate Control for AF

Agent		Acute (IV)	Maint. (PO)	Comments
CCB	**Verapamil**	5-10 mg over 2′ may repeat in 30′	120-360 mg/d in divided doses	↓ BP (Rx w/ Ca gluc) Can worsen HF Preferred if severe COPD Can ↑ dig levels
	Diltiazem	0.25 mg/kg over 2′ may repeat after 15′ 5-15 mg/h infusion	120-360 mg/d in divided doses	
βB	**Metoprolol**	2.5-5 mg over 2′ may repeat q5′ × 3	25-100 mg bid or tid	↓ BP (Rx w/ glucagon) Preferred if CAD Risks: HF & bronchospas.

Digoxin* (onset >30 min)	0.25 mg q2h up to 1.5 mg	0.125-0.375 mg qd (adj for CrCl)	Consider in HF or low BP Poor exertional HR ctrl
Amiodarone	300 mg over 1 h → 0.5-1 mg/min × 24 h	100-200 mg QD	Consider in HF or low BP Long-term potential tox

IV βB, CCB and digoxin ***contraindicated*** if evidence of WPW (ie, pre-excitation or WCT) since may facilitate conduction down accessory pathway leading to VF; ∴ use procainamide, ibutilide or amiodarone

*Many meds incl. amio, verapamil, quinidine, propafenone, macrolides & azole antifungals ↑ digoxin levels.

Cardioversion

- Consider pharm or electrical cardioversion w/ 1st AF episode or if sx; if AF >48 h, 2-5% risk stroke w/ cardioversion (*pharmacologic or electric*) ∴ either TEE to r/o thrombus or ensure therapeutic anticoagulation for ≥3 wk prior if need to cardiovert urgently, anticoagulate acutely (eg, IV UFH)
- Likelihood of success ∝ AF duration & atrial size; control precip. (eg, vol status, thyroid)
- Consider pre-Rx w/ antiarrhythmic drugs (eg, ibutilide), espec if 1st cardioversion fails
- For pharmacologic cardioversion, class III and IC drugs have best proven efficacy
- If SR returns (spont. or w/ Rx), atria may be *mech. stunned;* also, high risk of recurrent AF over next 3 mo. ∴ **Anticoag postcardioversion ≥ 4 wk** (? unless <48 h and low risk).

Rhythm control (*Lancet* 2012;379:648; *Circ* 2014;130:2071)

- No clear survival benefit or ↓ stroke risk vs rate control (*NEJM* 2002;347:1825 & 2008;358:2667)
- Consider if *symptomatic* w/ rate control (eg, heart failure), difficult to control rate, or tachycardia-mediated cardiomyopathy

Antiarrhythmic Drugs (AAD) for AF (*Circ* 2011;123:104 & 2012;125:381; *EHJ* 2012;33:2719)

Agent	Conversion	Maintenance	Comments
Amiodarone	5-7 mg/kg IV over 30-60′ → 1 mg/min, 10 g load	200-400 mg qd (most effective AAD for SR)	↑ QT, but TdP rare Low rate of acute conversion. May convert wks after load, ∴ attention to anticoag Pulm, liver, thyroid toxicity ✓ PFTs, LFTs, TFTs Potentiates warfarin, ∴ → warfarin by ˜50%
Dronedarone	n/a	400 mg bid	↓ side effects but also ↓ effic. c/w amio;

				contraindic. in perm AF or sx HF / ↓ EF; risk of liver toxicity
III				
	Ibutilide	1 mg IV over 10′ may repeat × 1	n/a	Contraindic. if ↓ K or ↑ QT ↑ QT, 3-8% risk of TdP Mg 1-2 g IV to ↓ risk TdP Lasts 4-6 h
	Dofetilide	500 mcg PO bid	500 mcg mg bid	↑ QT, ↑ risk of TdP; renal adj
	Sotalol	n/a	80-160 mg bid	✓ for ↓ HR, ↑ QT; renal adj
	Flecainide	300 mg PO × 1	100-150 mg bid	PreRx w/ AVN blocker *Contraindic. if structural or ischemic heart disease*
IC				
	Propafenone	600 mg PO × 1	150-300 mg tid	
IA	Procainamide	10-15 mg/kg IV over 1 h	n/a	↓ BP; ↑ QT ± PreRx w/ AVN blocker

Underlying disease	**Maintenance AAD of choice**
None or minimal (incl HTN w/o LVH)	class IC (“pill in pocket”), sotalol, dronedarone
HTN w/ LVH	amiodarone
CAD	sotalol, dofetilide, amiodarone, dronedarone
HF	amiodarone, dofetilide

Radiofrequency ablation (*JAMA* 2015;314:278)

- **Rationale:** Controlling triggers in pulmonary veins can control AF when little atrial scar present. As progress to persistent and permanent, LA substrate more complex due to scarring and is likely harder to ablate with pulmonary vein isolation alone.
- **Indication:** reasonable alternative to AAD in structurally normal heart
- **Approach:** for paroxysmal AF, circumferential pulm. vein isolation done via ablation in LA myocardium (ablation in PVs causes stenosis) w/ ~80% success (*Lancet* 2012;380:1509). In AF w/o ↑ ↑ LA or ↓ EF, RFA still superior to AAD, but lower success rate w/ AF recurring in ~1/2 over 2 y and 2nd RFA often required to prevent LA flutter (*NEJM* 2012;367:1587; *JAMA* 2014;311:692). Utility of upfront additional lines of block unclear (*NEJM* 2015;372:1812).
- Often performed on uninterrupted/minimally interrupt. warfarin or Xa inhib (*Circ* 2014;129:1688)

- **Risks and complications**

  → arrhythmia & pericarditis during healing post ablation

  left atrial flutters may persist and need additional "touch up" ablation

  rarer complications (1-2%): stroke, tamponade, phrenic nerve injury, PV stenosis, LA-esophageal/mediastinal communication (˜3 wk after procedure, severe dysphagia, fever, CNS signs of thromboembolism; dx w/ CT scan or barium study, *no* TEE*; emergent* thoracic surgery)

- Surgical "maze" procedure (70-95% success rate) option if undergoing cardiac surgery

Oral anticoagulation (*Circ* 2014;130:2071; *JAMA* 2015;313:1950)

- *All valvular* AF (ie, rheum MS, valve prosthesis or repair), as stroke risk very high
- Nonvalvular AF (NVAF): stroke risk ˜4.5%/y, but varies depending on patient; anticoagulation → 68% ↓ stroke but carries risk of bleeding; ∴ use a risk score to guide Rx
- **CHA_2DS_2-VASc: C**HF (1 point), **H**TN (1), **A**ge ≥75 y (2), **D**M (1), **S**troke/TIA (2), **V**ascular disease (MI, PAD, or aortic plaque) (1), **A**ge 65-74 y (1), ♀ **S**ex **c**ategory (1) annual risk of stroke (*Lancet* 2012;379:648): at low end, ˜1% per point: 0 → ˜0%, 1 → 1.3%, 2 → 2.2%, 3 → 3.2%, 4 → 4.0%; at higher scores, risk ↑ ↑ (5 → 6.7%, ≥6 → ≥10%)
- Anticoagulation recommendations: **score ≥2 → anticoagulate**

  score 1 → consider anticoagulation or antiplatelet Rx (? latter reasonable if risk factor 65-74 y, vasc disease or ♀) or no Rx

  score 0 → reasonable to not anticoagulate
- **HAS-BLED** (*Chest* 2010;138:1093)

  HTN (1 point if >160 mmHg), **A**bnl renal/liver fxn (1 for each), **S**troke (1), **B**leeding hx or predisposition (eg, anemia), **L**abile INR (time in therapeutic range <60%), **E**lderly (eg, age >65, frailty), **D**rugs/alcohol concom (1 point for antiplt or NSAID; 1 for alcohol)

  ≥3 → ↑ risk for bleeding, ∴ consider closer monitoring or different drug/dose selection
- Special situations in Pts w/ indication for anticoagulation:

  plan for rhythm control: continue anticoagulation

  Pt refuses anticoag: ASA + clopi or, even less effective, ASA alone (*NEJM* 2009;360:2066) underwent PCI: ? Rx w/ anticoagulant & clopidogrel, omit ASA (*Lancet* 2013;381:1107)
- **Anticoagulant options: factor Xa or direct thrombin inhib** (NVAF only) or **warfarin** (INR 2-3; w/ UFH bridge if high risk of stroke)
- Periop rate of arterial embolization in AF (w/o mech valve) <0.5%; Ø benefit to bridging anticoag w/ LMWH & ↑ bleeding c/w stopping warf 5 d before (*NEJM* 2015;373:823)

Novel Oral Anticoagulants for Nonvalvular AF

Anticoag	Dosing	Efficacy & safety vs warfarin

Dabigatran (Direct thromb inhib)	150 mg bid (110 not avail in U.S.) (75 mg bid if CrCl 15-30)	150 mg: ↓ ischemic stroke & ICH 110 mg: ≈ ischemic stroke & ↓ major bleed/ICH Risks: GI side effects, ↑ MI c/w warfarin
Rivaroxaban (FXa inhib)	20 mg qd (15 mg qd if CrCl 15-50) w/ pm meal	≈ ischemic stroke & ↓ major bleed incl ICH
Apixaban (FXa inhib)	5 mg bid (2.5 mg bid if ≥2 risks: ≥80 y, ≤60 kg, Cr ≥1.5 mg/dL)	≈ ischemic stroke & ↓ major bleed incl ICH, 11% ↓ death. In Pts felt not cand for warfarin, apixa 55% ↓ stroke w/o ↑ bleed vs ASA alone.
Edoxaban (Fxa inhib)	60 mg qd if CrCl 51-95 (30 mg if CrCl 15-50) (30/15 mg regimen not available in U.S.)	60/30 mg: ≈ ischemic stroke & ↓ major bleed incl ICH, 14% ↓ CV death 30/15 mg: ↑ ischemic stroke & ↓ ↓ major bleed incl ICH, 15% ↓ CV death

- Rapid onset (w/in several hrs) and offset. Consequently do not need to bridge when starting. However, missing 1 dose could lead to inadequate protection.
- No monitoring required
- Require dose adjustment based on renal fxn, which should be monitored while on drug
- Difficult to reverse if bleeding. Prothrombin complex concentrate or recombinant FVIIa needed. Dabi can be reversed w/ idarucizumab (Ab frag; *NEJM* 2015;373:511).

(*NEJM* 2009;361:1139; 2011;364:806; 365:883 & 981; 2013;369:2063; *Lancet* 2014;383:955)

Nonpharmacologic stroke prevent (ACC/HRS/SCAI 2015 Overview, *JACC* 2015)

- Percutaneous occlusion of left atrial appendage (LAA) w/ watchman device (nitinol cage w/ polyethylene membrane). Postprocedure: warfarin × ˜45 d followed by clopi × ˜4.5 mo and ASA lifelong. In NVAF w/ $CHADS_2$ ≥1-2, c/w warfarin, ≈ stroke (↓ hemorrhagic, ↑ ischemic), ≈ bleeding (↑ procedural, ↓ non-proc), ↓ CV death (*JACC* 2015;65:2614). Does not address issue of high-risk anticoag Pt w/ *existing* LAA thrombus.
- Epicardial snare to ligate LAA (lariat device). High rate of initial technical success (*JACC* 2013;62:108), but long-term clinical outcomes & safety to be defined.
- Surgical LAA resection reasonable if another indication for cardiac surgery. Resection superior to ligation, which can recanalize.

Atrial flutter

- Macroreentrant atrial loop typically involving cavotricuspid isthmus (usually counter-clockwise w/ flutter waves ⊖ in inf leads & ⊕ in V_1, but can be clockwise).
- Risk of stroke similar to that of AF; ∴ same mandate for stroke prevention.
- Ablation of cavotricuspid isthmus has 95% success rate w/ only 0.5% complication rate. Pts remain at risk for atrial fibrillation.

WIDE-COMPLEX TACHYCARDIA (WCT)

Etiologies (*Lancet* 2012;380:1520)

- **Ventricular tachycardia (VT):** accounts for 80% of WCT in unselected population
- **SVT conducted with aberrancy:** either fixed BBB, rate-dependent BBB (usually RBBB), conduction via an accessory pathway or atrially triggered ventricular pacing

Monomorphic ventricular tachycardia (MMVT)

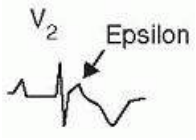
- All beats look similar; predominantly upward in V_1 = RBBB-type vs downward = LBBB-type
- Most commonly in obviously ***structurally abnormal heart*: prior MI** (scar); **CMP**

  mechanism is most commonly re-entry around areas of electrically silent scar tissue with slow myocardial conduction through adjacent areas of surviving myocytes

  focal arrhythmias also occur (RVOT, Ao root, fascicles, papillary muscles)

  re-entry utilizing the Purkinje system is also seen (Bundle Branch Reentry); "typical" form occurs in Pts w/ LBBB in sinus and VT w/ very similar morphology to sinus

- May occur in ***apparently* nl *heart that is actually diseased:***



  Arrhythmogenic (RV) CMP (ACM, qv): incomplete RBBB, ε wave (terminal notch in QRS) & TWI in V_1-V_3 on resting ECG, LBBB-type VT, dx w/ MRI (*Lancet* 2009;373:1289)

  subtle HCMP sarcoid; myocarditis (incl giant cell); anom coronary

- In structurally ***normal heart*** w/ nl resting ECG (prog generally good):

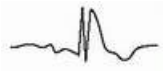
  RVOT VT: LBBB-type VT w/ inferior axis; often seen immediately after exercise; can suppress with CCB or βB or ablate

  idiopathic LV VT: RBBB-type VT w/ superior axis; responds to verapamil or can ablate

Polymorphic ventricular tachycardia (PMVT)

- QRS morphology and/or axis changes from beat to beat
- Etiologies: **ischemia; CMP**

  torsades de pointes (TdP = "twisting of the points," PMVT + ↑ QT): ↑ QT ***acquired*** (meds, lytes, stroke; see "ECG") w/ risk ↑ w/ ↑ HR, freq PVCs (pause dependent) *or* ***congenital*** (K/Na channelopathies) w/ resting Tw abnl & TdP triggered by sympa-thetic stimulation (eg, exercise, emotion, sudden loud noises) (*Lancet* 2008;372:750)

  Brugada syndrome (Na channelopathy): ♂ > ♀; pseudo-RBBB  w/ STE in V_1-V_3 (provoked w/ class IA or IC) on resting ECG

  catecholaminergic (CPVT): familial; mutations in ryanodine receptor or calsequestrin 2; presents during emotional or physical stress

Diagnostic clues that favor VT (assume until proven otherwise)

- **Prior MI, CHF** or **LV dysfxn** *best predictors* (90%) that WCT is VT (*Am J Med* 1998;84:53)

- Hemodynamics and rate do *not* reliably distinguish VT from SVT
- MMVT is regular, but may have initial "warmup period" and may be slightly irregular (as compared w/ SVT, which is extremely regular); *grossly* irregularly irregular rhythm suggests PMVT or AF w/ aberrancy
- More the QRS morphology is like QRS morphology in SR, more likely SVT
- ECG features that favor VT (*Circ* 1991;83:1649; *EHJ* 2007;28:589)

  AV *dissociation* (independent P waves, capture or fusion beats) proves VT; physical exam correlates: variable S_1 and cannon *a* waves on JVP

  very wide QRS (> 140 ms in RBBB-type or > 160 in LBBB-type)

  extreme axis deviation; RBBB-type w/ LAD; LBBB-type w/ RAD; shift in axis >40°; initial R wave in aVR

  QRS morphology atypical for BBB

  RBBB-type: absence of tall R′ (or presence of monophasic R) in V_1, r/S ratio <1 in V_6

  LBBB-type: onset to nadir >60-100 ms in V_1, q wave in V_6 longest RS interval in any precordial lead > 100 ms and R wider than S ratio of voltage Δ in initial 40 msec to Δ in terminal 40 ms ≤1

  concordance (QRS in all precordial leads w/ same pattern/direction)

Acute management

- If stable: conscious sedation & sync cardioversion; if unstable (↓ BP, angina, ΔMS, HF): emergent cardioversion; if pulseless → ACLS w/ CPR & cardioversion
- Refractory: consider amiodarone, procainamide, and lidocaine (if suspect ischemia)
- If suspect PPM-mediated tachycardia → place magnet (switches device to VOO or DOO)
- If ICD: should deliver Rx, but do not rely on for VT resolution. If stable, can interrogate ICD. If repeated, appropriate & successful shocks → antiarrhythmics to suppress arrhythmia. If repeated shocks (approp or inapprop) w/o arrhythmia term → disable device (magnet).

Long-term management (*JACC* 2006;48:1064)

- Workup: **echo** to ✓ LV fxn, **cath** or **stress test** to r/o ischemia, ? MRI and/or RV bx to look for infiltrative CMP or ARVC, ? **EP study** to assess inducibility

- **ICD:** 2° prevention after documented VT/VF arrest (unless due to reversible cause) 1° prev. if high risk, eg, EF <30-35%, ACM, Brugada, certain LQTS, severe HCM. See "Cardiac Rhythm Management Devices." ? Wearable vest if reversible etiology while waiting for ICD (*Circ* 2013;127:854).

  Antitachycardia pacing (ATP = burst pacing faster than VT) can terminate VT w/o shock
- **Meds:** βB, antiarrhythmics (eg, amio, mexiletine) to suppress VT, which could trigger shock
- If med a/w TdP → QT >500 ± VPBs: d/c med, replete K, give Mg, ± pacing (*JACC* 2010;55:934)
- **Radiofrequency ablation** if isolated VT focus or if recurrent VT triggering ICD firing; ablation before ICD implantation ↓ discharge rate by 40% (*Lancet* 2010;375:31)

SUDDEN CARDIAC DEATH (SCD)

Definition

- Sudden cessation of cardiac activity with hemodynamic collapse
- Technically sudden cardiac arrest (SCA) or "aborted SCD" if resuscitated
- Frequently due to sustained VT/VF

Etiologies

- **Coronary artery disease** (~60-70%)

  acute ischemia: ACS; spasm; congenital coronary artery anomaly

  scar from prior MI
- **Structurally abnormal heart or vasculature** (~10-15%)

  cardiomyopathy: DCM, HCM, ACM; myocarditis

  valvular heart disease

  myocardial rupture, tamponade, Ao dissection

  PE
- **Apparently structurally normal heart** (~10-15%)

  LQTS (acquired or congenital); Brugada syndrome; catecholaminergic polymorphic VT

  ACM or infiltrative cardiomyopathy

  Wolff-Parkinson-White (typically w/ antegrade conduction of AF → VF)

  complete heart block

  commotio cordis (*NEJM* 1995;333:337)

Precipitants

- Ischemia
- Drugs: antiarrhythmics, QT-prolonging, diuretics
- Electrolytes (usually not sufficient to cause SCD; always search for underlying cause)

Workup (*JACC* 2006;48:1064)

- Hx (usually very limited): may have had prodrome c/w ACS or HF; PMH; meds; FHx
- Exam: signs of cardiovascular disease
- ECG: ischemia, infarction, conduction block, QT, pre-excitation, abnormal V_1-V_3 (eg, pseudo-RBBB + STE, ε wave + TWI), LVH
- Echocardiogram; MRI if echo unrevealing and no other obvious cause
- Coronary angiography (? or CT angio)

  if STE or ? chest pain prodrome, urgent angio (unless poor neurologic prognosis)

  even w/o STE, 33-40% will have evidence of acute occlusion (*NEJM* 1997;336:1629 & *JACC Intv* 2015;8:1031)

- EP study (qv) if above workup unrevealing, programmed stimulation to look for accessory pathway, drug infusions to provoke arrhythmia from CPVT, LQTS, Brugada
- Exercise testing to provoke CPVT or assess resolution of pre-excitation to risk stratify WPW
- If genetic or unexplained SCD, evaluation of family members

SYNCOPE

Definition

- Sudden transient loss of consciousness due to global cerebral hypoperfusion
- If CPR or cardioversion required, then SCD (qv) and not syncope (different prognosis)
- Presyncope = prodrome of light-headedness without LOC

Epidemiology

- Incidence ↑ w/ age, particularly above 70 y; similar in men & women
- Lifetime incidence ~1 in 3

Etiologies (*NEJM* 2002;347:878; *JACC* 2006;47:473; *EHJ* 2009;30:2631)

- **Neurocardiogenic** (a.k.a. vasovagal, ~25%; *NEJM* 2005;352:1004)

  ↑ sympathetic tone → vigorous contraction of LV → mechanoreceptors in LV trigger ↑ vagal tone (hyperactive Bezold-Jarisch reflex) → ↓ HR (cardioinhibitory) and/or ↓ BP (vasodepressor)

  cough, deglutition, defecation, & micturition → ↑ vagal tone and thus can be precipitants

  carotid sinus hypersensitivity is a related disorder w/ an exaggerated vagal resp to carotid massage

- **Cardiovascular** (~20%, more likely in men than women)

  Arrhythmia (15%): challenging to dx as often transient

  Bradyarrhythmias: SSS, high-grade AV block (Stokes-Adams attack), ⊖ chronotropes, PPM malfunction

  Tachyarrhythmias: VT, SVT (syncope rare unless structural heart disease or WPW)

  Mechanical (5%)

  Endocardial/Valvular: AS, MS, PS, prosthetic valve thrombosis, atrial myxoma

  Myocardial: outflow obstruction from HCMP (can also cause VT), MI (more likely VT)

  Pericardial: tamponade

  Vascular: PE, PHT, aortic dissection, ruptured AAA, subclavian steal

- **Orthostatic hypotension** (~10%) hypovolemia/diuretics, deconditioning; vasodilat. (espec if combined w/ ⊖ chronotropes) autonomic neuropathy

  1° = Parkinson's, Shy-Drager, Lewy body dementia, postural orthostatic tachycardia syndrome (POTS, dysautonomia in the young)

  2° = DM, EtOH, amyloidosis, CKD (*NEJM* 2008;358:615)

- **Neurologic** (~10%): vertebrobasilar insufficiency (occlusion, dissection or steal), impaired perfusion to all

cerebral vessels (very rare), SAH

- Remainder of cases with unknown etiology
- Misc. causes of LOC (but not syncope): seizure, TIA/stroke, migraine, hypoglycemia, hypoxia, anemia, anaphylaxis, narcolepsy, psychogenic

Workup (etiology cannot be determined in ˜40% of cases)

- *H&P incl. orthostatic* VS *have highest yield and most cost-effective* (*Archives* 2009;169:1299)
- **History** (from Pt and *witnesses* if available) activity and posture before the incident precipitating factors:

  exertion → AS, HCMP PHT

  positional Δ → orthostatic hypotension

  stressors such as sight of blood, pain, emotional distress, fatigue, prolonged standing, warm environment, N/V, cough/micturition/defecation/swallowing ↑ vasovagal

  head turning or shaving → carotid sinus hypersensitivity arm exercise → subclavian steal

  prodrome: sx such as diaphoresis, nausea, blurry vision for >˜5 sec suggests vasovagal; abrupt onset suggests cardiac or seizure

  associated sx: chest pain (MI), palpitations (tachycardia)

  neuro: aura prior to event, neuro sx, postictal state, bowel/bladder incontinence, & lateral tongue biting suggestive of seizure; brief convulsive activity for < 10 sec may occur w/ syncope & mimic seizure, but true tonic then clonic activity is indicative of seizure
- **PMH:** prior syncope, previous cardiac or neurologic dis.; no CV disease at baseline → 5% cardiac, 25% vasovagal; CV disease → 20% cardiac, 10% vasovagal (*NEJM* 2002;347:878)
- **Medications that may act as precipitants** vasodilators: α-blockers, nitrates, ACEI/ARB, CCB, hydralazine, phenothiazines, antidep. diuretics; ⊖ chronotropes (eg, βB and CCB)

  proarrhythmic or QT prolonging: class IA, IC or III antiarrhythmics (see "ECG") psychoactive drugs: antipsychotics, TCA, barbiturates, benzodiazepines, EtOH
- **Family history:** CMP, SCD, syncope (vasovagal may have genetic component)

- **Physical exam**

  VS including *orthostatics* (⊕ if supine → standing results in >20 mmHg ↓ SBP, >10 mmHg ↓ DBP, or > 10-20 bpm ↑ HR), BP in both arms

  persistently abnormal VS *concerning*

  cardiac: HF (↑ JVP, displ. PMI, S_3), murmurs, LVH (S_4, LV heave), PHT (RV heave, ↑ P_2)

  vascular: ✓ for asymmetric pulses, carotid/vertebral/subclavian bruits

  carotid sinus massage to assess for carotid hypersensitivity (if no bruits and no h/o TIA or stroke); ⊕ if asystole >3 sec or ↓ SBP >50 mmHg

  neurologic exam: focal findings, evidence of tongue biting; FOBT
- **ECG** (abnormal in ˜50%, but only definitively identifies cause of syncope in <10%)

  Conduction abnl: SB <40 bpm, repetitive sinus pauses >3 sec, AVB (partic. Mobitz II 2° or 3°), IVCD or BBB

(partic. bifascicular block or alternating BBB) (*EHJ* 2009;30:2631)

Arrhythmia: ectopy, ↑ (or ↓) QT, preexcitation (WPW), Brugada, ε wave (ACM), SVT/VT Ischemic changes (new or old): atrial or ventricular hypertrophy

- Place on telemetry while diagnostic workup ongoing
- Lab: glc, Hb, preg test (child-bearing age ♀), ? D-dimer, ? troponin (low yield w/o other s/s)

Life-threatening dx

- *Arrhythmia:* VT, high-grade AVB, long sinus pauses
- *Cardiovascular structural disease:* critical AS, HCMP tamponade, aortic dissection, PE
- *Massive hemorrhage* (eg, large GIB, Ao rupture, splenic rupture, ectopic preg, RP bleed)
- *Neurologic:* SAH (headache + syncope)

High-risk features (*J Emerg Med* 2012;42:345)

- Advanced age (? >60 y), h/o CAD, HF/CMP, valvular or congenital heart disease, arrhythmias, or FHx SCD
- Syncope c/w cardiac cause (lack of prodrome, exertional, supine, or resultant trauma) or recurrent syncope (risk of recurrence if ≥2 prior episodes >50%)
- Complaint of chest pain or dyspnea; abnl VS or cardiac, pulmonary or neuro exam
- Abnormal ECG suggesting arrhythmia, conduction abnormality, ischemia/infarction; Pt w/ PPM/ICD (unless interrogated and found to have no arrhythmia)

Disposition

- High-risk Pts should usually be admitted w/ telemetry and further testing (qv)
- Low-risk Pts may be discharged with follow-up testing
- Obvious vasovagal syncope can be discharged

Other diagnostic studies (consider based on results of H&P and ECG)

- Ambulatory ECG monitoring: if suspect arrhythmogenic syncope

  Holter monitoring (continuous ECG 24-48 h): useful if *frequent* events arrhythmia + sx (4%); asx but signif. arrhythmia (13%); sx but no arrhythmia (17%)

  Event recorder (activated by Pt to record rhythm strip): limited role, as only useful if established prodrome (because must be Pt activated)

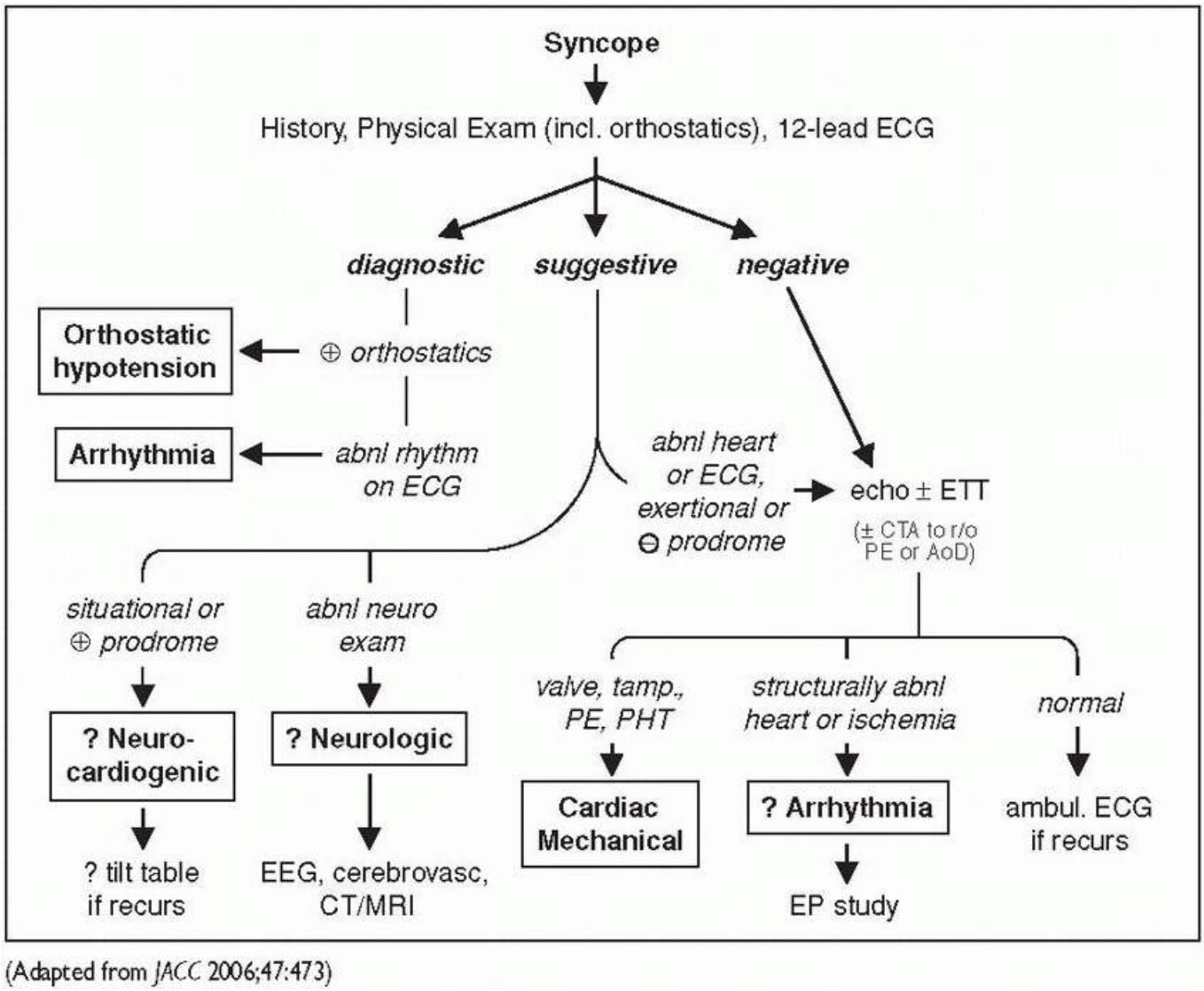
  External intermittent loop recorders (continuously saves rhythm, ∴ can be activated *after* an event): useful for episodes (including w/o prodrome) likely to occur w/in 1 mo

  Implantable loop recorders (inserted SC; can record up to 3 y): useful for infrequent episodes (< 1/mo); recommended for recurrent syncope w/o prodrome. Appears to establish a dx (often bradycardia) more frequently (55% vs 19%) than conventional testing (external loop recorder, tilt table, etc.; *Circ* 2001;104:46)
- Echo: consider to r/o structural heart disease (eg, CMP [incl HCMP & ACM], valvular disease [incl AS, MS, MVP], myxoma, amyloid, PHT, ± anomalous coronaries)
- ETT: espec w/ exertional syncope; r/o ischemia- or catecholamine-induced arrhythmias

- Cardiac catheterization: consider if noninvasive tests suggest ischemia
- Electrophysiologic studies (EPS, qv): consider in high-risk Pts in whom tachy or brady etiology is strongly suspected but cannot be confirmed;

  50% abnl (inducible VT, conduction abnormalities) if heart disease, but ? significance

  3-20% abnl if abnl ECG; <1% abnl if normal heart and normal ECG (*Annals* 1997;127:76)
- ? Tilt table testing: utility is debated due to poor Se/Sp/reproducibility; consider only if vasovagal dx suspected but cannot be confirmed by hx
- Cardiac MRI: helpful to dx ARVC if suggestive ECG, echo (RV dysfxn) or ⊕ FHx of SCD
- Neurologic studies (cerebrovascular studies, CT, MRI, EEG): if H&P suggestive; low yield



(Adapted from *JACC* 2006;47:473)

Figure 1-10 Approach to syncope

Treatment

- Arrhythmia, cardiac mechanical or neurologic syncope: treat underlying disorder
- Vasovagal syncope (*Int J Cardiol* 2013;167:1906): benefit for midodrine, SSRI

  ? 16 oz of H_2O before at-risk situations (*Circ* 2003;108:2660)

No proven benefit w/ βB (*Circ* 2006;113:1164) or tilt training

No benefit w/ PPM in RCT comparing active pacemaker vs pacemaker programmed in backup mode only. However, guidelines permit implant if ≥3 episodes/2y & loop recorder w/ asystole >3 sec (*Circ* 2012;125:2566).

No data for fludrocortisone, disopyramide

- Orthostatic syncope: volume replete (eg, 500 mL PO q a.m.); if chronic → rise from supine to standing *slowly,* compressive stockings, midodrine, atomoxetine (HTN 2014;64:1235), fludrocortisone, high Na diet

Prognosis (*Ann Emerg Med* 1997;29:459; *NEJM* 2002;347:878)

- 22% overall recurrence rate if idiopathic, else 3% recurrence
- Cardiac syncope: 2-fold ↑ in mort., 20-40% 1-y SCD rate, median survival ˜6 y
- Unexplained syncope w/ 1.3-fold ↑ in mort., but noncardiac or unexplained syncope w/ nl ECG, no h/o VT, no HF, age <45 → low recurrence rate and <5% 1-y SCD rate
- Vasovagal syncope: Pts not at increased risk for death, MI or stroke
- ✓ state driving laws and MD reporting requirements. Consider appropriateness of Pt involvement in exercise/sport, operating machinery, high-risk occupation (eg, pilot).

ANTIARRHYTHMIC DRUGS (AAD)

Procainamide (class IA = moderate Na channel blocker)

Dose	10-15 mg/kg IV over 1 h; 1-2 g bid (oral form not available in U.S.)
Uses	Converting AF & maint. SR; emergent Rx of VT or WCT of ? etiology
Side effects	→ QT, TdP. HoTN (w/ IV use); lupus-like synd. Metab by hepatic N-acetylation. NAPA K channel blocker and renally cleared; ✓ proc & NAPA levels.

Quinidine (class IA = moderate Na channel blocker)

Dose	200-648 mg tid (slowly uptitrate); can be given IV
Uses	Prevention of VT (used mainly in refractory cases). Blocks I_{TO} (Rx VF storms in Brugada syndrome).
Side effects	→ QT, TdP. Diarrhea often limiting. Moderate anticholinergic effects. α blockade → HoTN. Tinnitus, hemolytic anemia, thrombocytopenia.

Disopyramide (Norpace) (class IA = moderate Na channel blocker)

Dose	200-600 mg bid (slowly uptitrate)
Uses	Rx for AF in HCMPP Rx for HCMPP(b/c ⊖ inotrope)
Side effects	→ QT, TdP. Marked anticholinergic effects. ⊖ inotrope (∴ contraindic in Pts w/ ↓ EF).

Lidocaine (class IB = mild Na channel blocker)

Mech	Blocks activated & inactivated but not resting Na channels; ∴ selectively blocks ischemic arrhythmogenic tissue
Dose	100 mg IVB, subsequent 50 mg IVB prn × 2; infusion 1-4 mg/min
Uses	Emergent treatment of VT/VF
Side effects	Δ MS, slurred speech, twitching; ✓ lido levels, toxicity can manifest as seizure
Other	**Mexiletine:** IB that can be given PO (200-300 tid) to suppress VT/VF

Flecainide (Tambocor) (class IC = marked Na channel blocker)

Dose	50-150 mg bid (slowly uptitrate); 200-300 mg × 1 (pill-in-pocket)
Uses	Maintenance of SR (PAF, PSVT); acute cardioversion (test in-hosp first!) PreRx with AV nodal blocker to prevent rapid ventricular conduction.
Side effects	→ mortality if structural heart disease (∴ *contraindic if ischemic or structural heart disease*). Metallic taste, negative inotropy.
Other	**Propafenone** (Rhythmol): similar indications & contrindic. Also βB. 150-300 mg tid or 225-425 bid (slowly uptitrate); 450-600 mg × 1 (pill-in-pocket).

Amiodarone (Cordarone) (class III = K channel blocker)

Mech	Primarily K channel blocker, but also Na channel blocker, βB, & CCB
Dose	IV load: 150 mg over 10 min → 1 mg/min × 6 h → 0.5 mg/min × 18 h → cont IV drip or Δ PO load for total ~10 g. PO load: 400 mg tid → total ~10 g Maintenance: 200 (for AF) to 400 (for VT) qd Emergent Rx of VT/VF: 300 mg IVB ± another 150 mg IVB if persists/recurs
Uses	Cardioversion of AF & maintenance of SR; treatment & suppression of VT/VF
Side effects	HoTN when given IV; bradycardia. Hypo- (~10%) or hyper- (~3%, typically in iodine-defic Pts) thyroidism. ↑ LFTs; pneumonitis or pulmonary fibrosis.
Other	**Dronedarone:** noniodine-containing derivative of amio w/ ↓ efficacy but better tolerability. Used for paroxysmal AF (400 mg bid). Contraindic if HF or perm AF.

Sotalol (Betapace) (class III = K channel blocker)

Mech	K+ blocker, and nonselective βB *d* and *l* isomers, respectively
Dose	Start 80 mg bid, ↑ to 120 and then up to 160 mg bid as needed.
Uses	Maintenance of SR in Pts w/ AF, prevention of VT in pts with ICD
Side effects	→ QT (contraindic if QTc >450 msec, adjust dose to keep <500 ms), TdP. ∴ monitor in hospital for ≥3 days on maintenance dose. Renally cleared.

Ibutilide (Corvert) (class III = K channel blocker)

Dose	1 mg IV over 10 min, may repeat × 1. Mg 2 g IV routinely during infusion.
Uses	Conversion of AF
Side effects	→ QT, TdP (~5%). Replete K & Mg before Rx. Continuous ECG monitoring (including for several hrs after last dose) and be prepared to defibrillate.
Other	**Dofetilide** (Tikosyn): maintenance of SR in Pts w/ AF. 0.5 mg bid. ↑ QT, TdP.

ELECTROPHYSIOLOGY STUDY (EPS)

Indications

- Syncope (w/ high-risk features or abnl ECG); identification of unsuspected tachyarrhythmias; distal

conduction disease (not good for ruling out paroxysmal sinus node dysfunction)

- Determination of mechanism of narrow [eg, AVNRT (dual AV node physiology), AVRT (bypass tract), ectopic atrial tachycardia] and wide complex tachycardias
- Diagnosis in Pts post cardiac arrest
- Risk stratification for SCD (ie, inducibility of VT/VF) in structural heart disease

Preprocedural evaluation

- Coronary angiography to r/o signif CAD (either as cause of ischemia-induced arrhythmia and/or to fix before inducing VT)
- TEE to r/o LA clot before left atrial procedures

Commonly used catheters and measurements

- Most often electrode catheters placed via femoral vein and placed at high right atrium (HRA), His bundle (HBE) and right ventricular apex (RVA). For SVT, also have a catheter in coronary sinus (CS), coursing to left side of heart around mitral annulus.

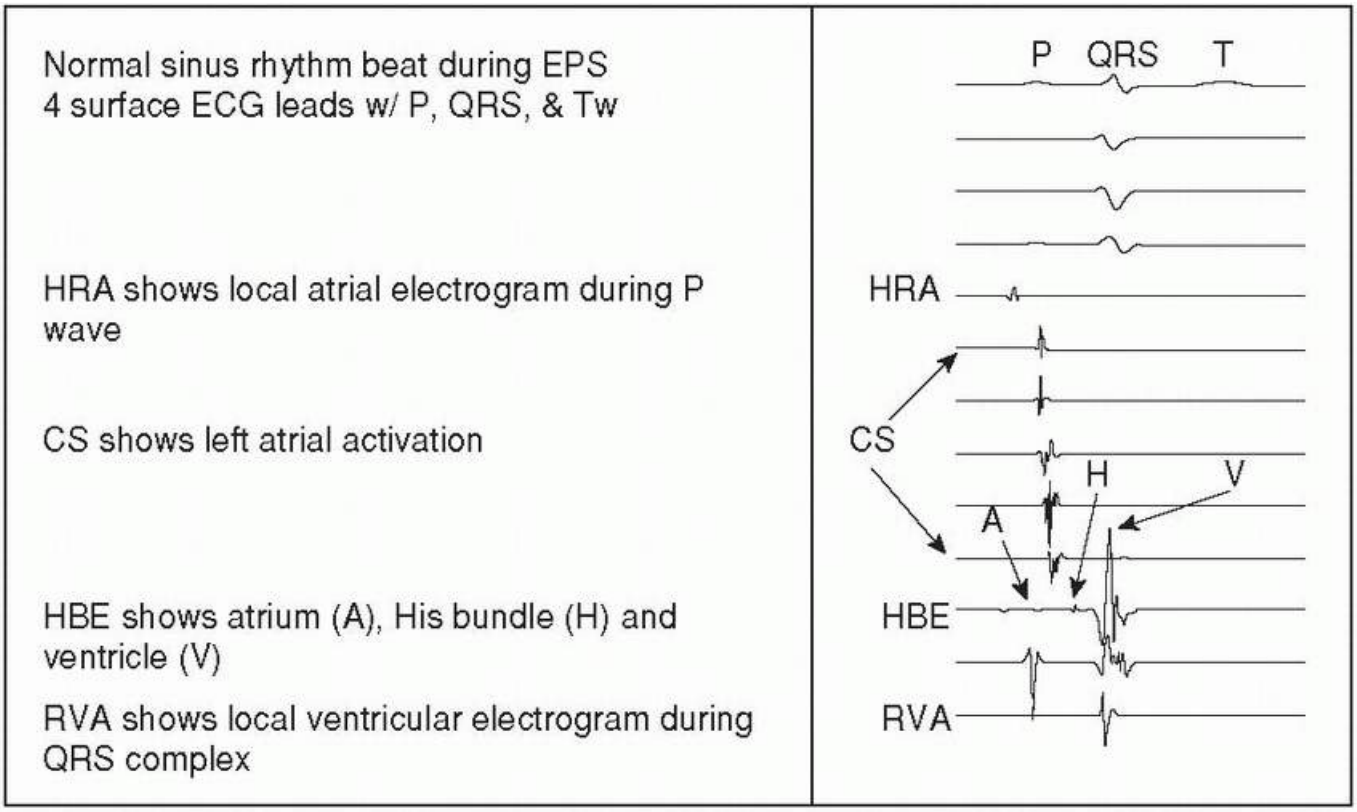


Figure 1-11 Tracing from EPS

- His bundle electrogram allows measurement of AVN conduction (AH interval) and distal conduction system (HV interval, nl 35-55 ms):

  HV interval <35 ms: pre-excitation (WPW)

  HV interval >35 ms: conduction system disease. LBBB typically 55-65 ms, > 70 ms w/ syncope needs PPM, > 100 ms needs PPM

- Current driven through electrodes used to pace heart and introduce extra beats following 8-beat drive train (programmed electrical stimulation, PES) usually done at HRA and RVA

- Atrial PES can be used to reveal evidence of dual AVN pathways or accessory pathways. Can also be used to induce SVT, AF, AFL.
- Ventricular PES can be used to reveal evidence of concealed accessory pathways, assess inducibility of VT/VF (and thereby risk of SCD), particularly in ischemic heart disease.
- Drug infusions (eg, epinephrine, procainamide) can help to dx LQTS, CPVT and Brugada

Complications

- Vascular injury at site of access
- Damage to tricuspid valve
- Arrhythmias
- Cardiac chamber perforation ± tamponade
- If ablation:

  heart block ± need for PPM

  chamber perforation ± tamponade for AF ablation: PV stenosis, phrenic nerve injury, atrio-esophageal fistula

CARDIAC RHYTHM MANAGEMENT DEVICES

Pacemaker Code

A, atrial; V, vent; O, none; I, inhibition; D, dual; R, rate-adaptive	1st letter	2nd letter	3rd letter	4th letter
	Chamber paced	Chamber sensed	Response to sensed beat	Program features

Common Pacing Modes

VVI	Ventricular pacing on demand w/ single lead in RV. Sensed ventricular beat inhibits V pacing. Used in chronic AF with symptomatic bradycardia.
DDD	A & V sensing/pacing (RA & RV leads). Native A beat inhib A pacing & *triggers V pacing* → tracking of intrinsic atrial activity. Maintains AV synchrony, ↓ AF.
Mode Switch	In atrial tachyarrhythmia (usually atrial flutter or fibrillation), pacemaker switches from DDD to nontracking mode (like VVI) in order to prevent pacing the ventricle at the upper rate limit (max rate at which PPM will pace ventricle) in an attempt to track the rapid atrial arrhythmia

Magnet (place over generator)	Pacemaker will pace at fixed rate regardless of intrinsic activity (= VOO/DOO). ICD: no detection/shock, but pacing programming preserved. Indications: ✓ ability to capture; ✓ battery life (to which rate will be proportional; uses less energy than programmer and does not require a programmer); during surgery w/ electrocautery; hemodynamic instability due to inappropriate PPM inhib, failure to mode switch or PM-mediated tachy; inapprop ICD shocks.

Indications for Permanent Pacing (*Circ* 2012;126:1784)

AV block	3° or type II 2° AVB a/w sx or w/ either HR <40 or asystole ≥3 sec (≥5 sec if in AF) while awake; ? asx 3° or type II 2° AVB; bifascicular or alternating left & right BBB
Sinus node	SB, pauses, chronotropic incompet a/w sx or ? if sx w/o clear assoc
Tachy-arrhythmia	Most common: AF w/ SSS, where pacing permits rate support of sinus rhythm in setting of rate controlling drugs for episodes of AF Pacing after AV junctional ablation for uncontrolled rates in AF Sustained pause-dependent VT Selected Pts w/ congenital long QT may benefit from pre-emptive pacing from their ICD
Syncope	Carotid sinus hypersensitivity with asystole >3 sec ? Neurocardiogenic syncope w/ prominent cardioinhib. response ? Syncope with bi/trifascicular block and not likely 2° to other causes

Pacing Complications (Pacemaker or ICD)

Issue	Manifestation	Description
Failure to pace	Bradycardia	Oversensing (ie, inappropriate inhibition) due to noise from lead fracture or set screw problem, myopotentials, EMI source outside body such as electrocautery or metal detector Sensitivity too low Battery depletion
Failure to capture	Pacing impulses delivered, but no P waves or QRS evoked	Elevated pacing threshold due to lead dislodgement, local tissue reaction or injury
Failure to sense	Inapprop. pacing	Lead dislodgment or disease of local myocardium (measured electrogram from leads too small to sense) or sensing threshold too high
PM-	WCT at device	Seen w/ DDD. VA retrograde conduction; sensed by A lead →

mediated tachycardia	upper rate	triggers V pacing → etc.
PM syndrome	Palpit, HF	Seen w/ VVI in Pts w/ intact AV conduction, due to loss of AV synchrony
SVC syndrome	Facial plethora	Thrombosis acutely or scarring a/w chronic intravascular lead(s)
Infection	Fever, ⊕ BCx	See below

Cardiac resynch therapy (CRT)/Biventricular (BiV) pacing (*Circ* 2012;126:1784)

- LBBB and standard RV apical pacing w/ resultant LBBB-like morphology causes dyssynchrony: LV septum activated before LV lateral wall. Wasted myocardial energy due to: prolonged time of contraction (sometimes continuing after AoV closure), sequential rather than simultaneous activation of papillary muscles → functional MR.
- 3-lead pacemaker (RA, RV, coronary sinus to LV lateral wall - LV lead can also be placed surgically by thoracotomy); pre-excites LV lateral wall in attempt to overcome dyssynchrony. R>S in V_1 & predominantly negative in I suggests approp LV capture. QRS width depends on degree of LV pre-excitation; can be narrower or wider than baseline.
- **Indications:** LVEF ≤35% + NYHA II-IV despite med Rx + SR + LBBB ≥150 (? ≥120) ms; mortality benefit only if LBBB (regardless of QRS width) (*NEJM* 2014;370:1694) can also consider in AF, but rate control or AVN ablation necessary to allow ventricular capture, as the greater proportion of time paced, the greater the CRT effect;

  ? NYHA I w/ LVEF ≤30% + LBBB ≥150 ms;

  ? EF ≤50% w/ AVB + indic for PPM (*NEJM* 2013;368:1585)
- **Benefits**

  acutely: simultaneous contraction of LV walls and reduction in MR

  after 3-6 mo: improvement in one NYHA class in 2/3 of Pts; some "super-responders" will normalize EF

  clinically: ↓ HF sx, ↓ HF hosp., ↑ survival (*NEJM* 2005;352:1539; 2010;363:2385)

  ineffective when LV lead location poor or LV scarring prevents pacing and/or improvements in wall motion

Implantable cardiac defibrillator (ICD) (*NEJM* 2003;349:1836; *JACC* 2009;54:747)

- RV lead: pacing and sensing like pacemaker lead, coils plus outside housing of ICD can participate in shocking circuit (± antitachycardia pacing [ATP] = burst pacing faster than VT rate to stop VT w/o painful shocks); ± RA lead for dual chamber pacing
- Uninterrupted warfarin at time of ICD (or PPM) placement ↑ risk of pocket hematoma vs bridging with UFH (*NEJM* 2013;368:2084)
- Subcutaneous ICD contains only shocking function (no ATP, no pacing) implanted in the left parasternal area with pulse generator in left lateral thoracic area. Reasonable for those with poor central access and those w/o

pacing requirement (*Circ* 2013;127:854).

- Wearable defibrillator vest can act as a “bridge” for Pts who cannot have an implanted defibrillator for weeks to a few months due to infection or other issue. Not yet demonstrated benefit as a bridge for those who do not yet meet guidelines for ICD (eg, early post MI or new NICMP (*JACC* 2013;62:2000). Data do not support home AED for these Pts either (*NEJM* 2008;358:1793).
- **Pt selection** (*NEJM* 2004;350:2151 & 351:2481; 2005;352:225; 2009;361:1427; *Circ* 2012;126:1784)

  2° prevention: survivors of VF arrest, unstable VT w/o reversible cause (*NEJM* 1997;337:1576); structural heart disease & spontaneous sustained VT (even if asx)

  1° prevention:

  LVEF ≤30% & post-MI *or* LVEF ≤35% & NYHA II-III *or* LVEF ≤40% & inducible VT/VF wait ≥40 d if post-MI, >9 mo after dx of NICM, or if presumed reversible; *however,* consider ICD if hemodyn signif VT/VF w/in window (& >48 h after AMI) (*Circ* 2014;130:94)

  consider for HCM, ARVC, Brugada, sarcoid, LQTS, Chagas or congenital heart disease if risk factors for SCD

  life expectancy must be > 1 y
- **Benefits:** ↓ mortality from SCD c/w antiarrhythmics or placebo
- **Risks:** inapprop shock in ~15-20% at 3 y (most commonly due to misclassified SVT); lead fracture
- ICD discharge: ✓ device to see if approp; r/o ischemia, other proximate cause; if recurrent VT, ? drug Rx (eg, amio + βB; *JAMA* 2006;295:165) or VT ablation (*NEJM* 2007;357:2657); ablation at time of ICD ↑ risk of VT by 40% (*Lancet* 2010;375:31)
- Telemonitoring may improve outcomes (*Lancet* 2014;384:583)

Device infection (*Circ* 2010;121:458; *JAMA* 2012;307:1727; *NEJM* 2012;367:842)

- Presents with one or more of the following: *pocket infection* (warmth, erythema, tenderness), *fever, bacteremia* and/or *sepsis*
- Incidence ~2% over 5 y; if *S. aureus* bacteremia, infxn in ≥35%
- More common a complication of generator change
- TTE/TEE used to help visualize complic. (eg, vegetation), but even ⊖ TEE does not r/o
- Treatment: abx and *removal of system* if evidence of pocket infection or GPC bacteremia (*Heart Rhythm* 2009;7:1085)
- Prophylaxis: no recommendation for routine abx prior to invasive procedure